



South Texas Veterans Healthcare System (STVHCS) Research Service Handbook for Human Research Investigators and Staff

2nd Edition: January 2009



STVHCS Investigators and Study Staff,

We hope that you find the STVHCS Research Service Handbook for Human Research Investigators and Staff a useful reference and a valuable source of information. Providing educational resources and up to date information regarding research activities for our investigators and study staff is of paramount importance to us.

The Investigator Handbook is designed to provide important guideposts to policies and procedures to assist with the conduct of research at the STVHCS. The handbook also provides information regarding where investigators and study staff can go to find more information or to have questions addressed. In addition to a printed format, the handbook is also available on line at the STVHCS Research website: <http://www.southtexas.va.gov/Research> under Investigator Resources. Please refer to the website for the most up to date version of the handbook.

We encourage you to contact us, or anyone else in the STVHCS Research & Development Office at anytime with any comments, suggestions, concerns, or questions regarding research.

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ACOS for Research and Development

Kimberly Summers, PharmD
Assistant Chief for Clinical Research

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SECTION 1: Research & Development Service Contacts

All STVHCS Research offices can be reached by dialing **(210) 617-5300** and then the extension listed. The Research Department is located on the second floor in the Q hallway.

Research Administration Offices:

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STVHCS Research Service Website:

The following information can be found at <http://www.south-texas.med.va.gov/research/>

SECTION 2: VA Research at the STVHCS

1. VA Research

The STVHCS research program aspires to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our veterans and the nation.

A research project is designated as "VA research" if it meets any of the following criteria:

- a. The project is supported by funds from VA Central Office or funds are administered by the Biomedical Research Foundation of South Texas (BRFST).
- b. Study personnel enroll human subjects, obtain informed consent, or carry out research procedures utilizing VA resources (e.g., CPRS, funds, facilities, space, personnel, equipment).
- c. VA paid employees, employees appointed to work without compensation (WOC), or an employee assigned to VA through the Intergovernmental Personnel Act (IPA) of 1970 work on the project as part of their official duties at the VA or during a designated VA tour of duty.
- d. The project recruits VA subjects (staff, patients, or volunteers).
- e. The research involves the use of the STVHCS's nonpublic information to identify or contact human research subjects or prospective subjects or to use such data for research purposes.

2. STVHCS Demographics

The STVHCS provides healthcare services to a population of over 85,000 veterans who live in the South Texas area. The STVHCS is comprised of the Audie L Murphy Medical Division, the Kerrville Division, and the Satellite Clinic Division. The Audie L Murphy is a 268 bed facility providing primary, secondary, and tertiary health care in medicine, surgery, psychiatry, and rehabilitation medicine. It also supports a 90 bed Extended Care Therapy Center, a 30-bed Spinal Cord Injury Center, an eight-bed Bone Marrow Transplant Unit, and a Geriatric Research, Education, and Clinical Center (GRECC). The Satellite Clinic Division includes a number of Community Based Clinics (CBOC) located throughout the region in Corpus Christi, McAllen, San Antonio, Laredo, Harlingen, and Victoria.

STVHCS treated 85,112 outpatients in fiscal year 2007. An additional 279 patients received inpatient care only. The ethnicity of the veterans served is 46% Caucasian, 42% Hispanic, 7% Black, and 1% Pacific Islander, inclusive of a 12% female population. Vietnam Era veterans account for nearly forty percent (39%) of all patients in the STVHCS. Additional eras of service include: Persian Gulf War (20%), World War II (10%), and Korean (8%). Twenty-four percent (24%) of STVHCS outpatients have diabetes. Other common conditions include: hypertension (44%), heart disease (16%), post-traumatic stress disorder (11%), and chronic obstructive pulmonary disease (10%).

3. STVHCS Research

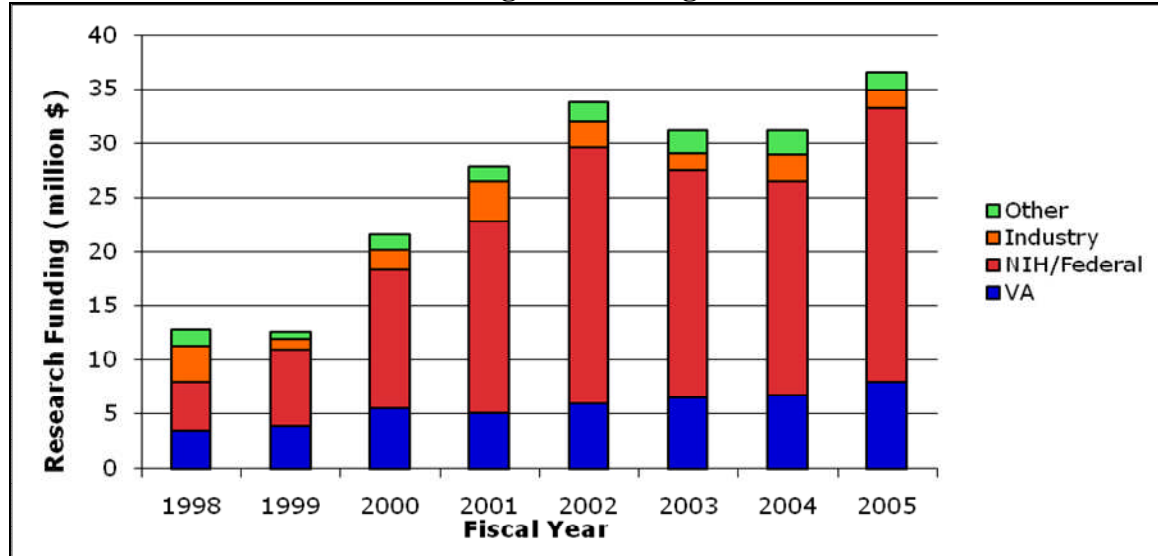
The STVHCS is a major resource for clinical and translational research in San Antonio. Ranked in the top 10 of VA research facilities (Table 1), the STVHCS Research Programs include Clinical Sciences Research (single-site and multi-site cooperative studies), Biomedical Laboratory Research, Health Services Research, and Rehabilitation Research. The research dollars which come into the STVHCS Research Program have consistently increased over the years (Figure 1). Currently there are approximately 400 active human protocols being conducted by over 150 investigators in the STVHCS. In Clinical Research there are 6 VA Cooperative Trials (prostate cancer, HIV, heart disease, diabetes, anticoagulation), 3 VA-funded Clinical studies (2 in diabetes, 1 in bipolar disease), 134 Pharmaceutical industry studies (cancer, HIV, mood disorders, diabetes, heart disease, lung disease), and 64 Investigational Drug studies. In Biomedical Laboratory Research there are 31 VA-funded studies and 23 NIH-funded studies. In addition, there are 2 VA Research Centers (Neurodegeneration and HIV/AIDS). There are approximately 60 approved animal protocols within the STVHCS. In Health Services Research there is a Research Enhancement Award Program with 16 Investigators (4 VA-funded) entitled the Veterans Evidence-based Research, Dissemination, and Implementation Center (VERDICT). The Rehabilitation program operates a fully equipped gait analysis laboratory to investigate the effects of prosthesis design on amputee recovery and functional status. The system dedicates 9,000 sq ft of space to the VERDICT, 35,000 sq ft of wet lab space, and 12,000 sq ft for animal research.

The Veterans Integrated Service Network (VISN) runs a New Investigator Award program. Thirty-one (31) new investigator awards have been made to STVHCS researchers since 1998; of these young investigators 70% have been successful in gaining future VA or NIH support.

TABLE 1. National VERA Ranking 2006

Ranking	Location	Dollars (1000s)
1	San Francisco	55,735
2	San Diego	42,645
3	Palo Alto	37,319
4	Baltimore	33,166
5	West Haven	31,829
6	Seattle	31,737
7	Iowa City	29,083
8	Portland	26,197
9	West Los Angeles	25,483
10	San Antonio	24,260
11	Decatur	22,285
12	Little Rock	22,257
13	Philadelphia	21,563
14	Durham	20,909
15	Minneapolis	20,210

FIGURE 1. STVHCS Research Program Funding



4. University of Texas Health Science Center at San Antonio (UTHSCSA) Affiliation

UTHSCSA serves as the medical school affiliate for STVHCS. The STVHCS is an important full partner in the research mission of the UTHSCSA, synergistically providing support for faculty and staff to conduct the studies needed to improve the health of Veterans and South Texans.

The STVHCS R&D Committee utilizes the UTHSCSA Institutional Review Board (IRB) per a Memorandum of Understanding (MOU). Before a research project involving humans as subjects can begin, it must be reviewed and approved by the IRB. The IRB has the responsibility of protecting the rights and welfare of human subjects. VA representatives are appointed to the UTHSCSA IRB by the Medical Center Director for a period of 3 years and may be re-appointed indefinitely. In order to assure the STVHCS interests are adequately represented, at least one VA member of the IRB must be present during the review of any VA research.

The STVHCS R&D Committee must approve all activities that engage the STVHCS in research. The investigator responsibilities at the STVHCS are in addition to any investigator responsibilities that must be adhered to when the research is approved by the affiliated UTHSCSA. Research may not be initiated at the STVHCS until written notice is received confirming both UTHSCSA IRB **AND** STVHCS R&D Committee approval.

5. Frederic C. Bartter General Clinical Research Center (GCRC)

Since 1982, the UTHSCSA has successfully managed a National Center for Research Resources (NCRR) funded GCRC in close collaboration with the STVHCS. The GCRC was established in the VA to pool local resources and create an economical clinical research program to serve both Veterans and non-Veterans from South Texas. The STVHCS-Audie Murphy Division houses the

GCRC on the seventh floor. The VA provides personnel to manage the GCRC through a sharing agreement with the UTHSCSA. Of the 35 full time employees affiliated with the GCRC, 20 of them are VA paid staff. The VA also dedicates 13,000 sq ft of space to the GCRC to conduct clinical research.

Because the San Antonio GCRC represents a joint venture shared by two federal agencies (the NIH and VA), and is administered by a state agency (the UTHSCSA), the fiscal arrangements and unit administration must conform to policies of VA Central Office, NIH, and the UTHSCSA. The per diem rate with this arrangement includes not only the actual bed costs but also the costs for paramedical personnel (e.g., nurses), ancillary tests, and unit administration (e.g., medical records).

The GCRC is a significant part of the clinical and translational research at the UTHSCSA and STVHCS. In 2002, the GCRC established a Research Imaging Core and a Biostatistics and Informatics Core that provide additional services to investigators on the UTHSCSA campus. The GCRC Research Subject Advocate has established a Data Safety and Monitoring Program using Total Quality Management principles that have become integrated into the STVHCS and UTHSCSA research compliance efforts.

SECTION 3: Human Research Protection Program (HRPP)

1. Definition of Research

Research is defined as an activity designed to develop or contribute to new generalizable knowledge through a process of hypothesis testing or data collection that permits conclusions to be drawn. Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective. Any prospective or retrospective collection of clinical data with the intent to contribute to generalizable knowledge constitutes research. Examples of such clinical data collection would include data collected for research seminars, posters, abstracts, manuscripts, and pilot data.

The FDA defines research as a clinical investigation. A clinical investigation refers to any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the FDA or is not subject to requirements for prior submission to the FDA, but the results of which are intended to be submitted later to, or held for inspection by the FDA as part of an application for research or marketing permit.

If you would like additional information or have any questions regarding the definition of research please contact the STVHCS R&D office at (210) 617-5123.

2. Definition of Human Subject

A human subject is an individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through the use of identifiable private information. An intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

The FDA defines a human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. This definition also includes an individual on whose specimen an investigational device is used.

3. Definition of Human Subject Research

Human subject research includes all research meeting the definition of "research" performed with "human subjects" as defined above.

For additional information regarding human subject research and to determine if your protocol constitutes human subjects research refer to Appendix A. If you have additional questions regarding whether or not an activity is consider human subject research please contact the UTHSCSA IRB Director at (210) 567-2357 or the STVHCS R&D office at (210) 617-5123.

4. “Engaged” in Human Subject Research

An institution is engaged in human subject research whenever its employees or agents: intervene with living individuals by performing invasive or noninvasive procedures for research purposes; manipulate the environment for research purposes, interact with living individuals for research purposes or obtain, release, or access individually-identifiable private information for research purposes.

5. Ethical Principles Governing Research

STVHCS abides by the ethical principles governing research involving human subjects, which are provided in the Nuremberg Code, the Declaration of Helsinki and the Belmont Report. All activities related to human subject research, regardless of funding source, are guided by these ethical principles.

- A. **Nuremberg Code:** addresses the necessity of requiring the voluntary consent of the human subject and the concept that any individual “who initiates, directs or engages in the experiment” must bear personal responsibility for ensuring the quality of consent.
- B. **Declaration of Helsinki:** calls for prior approval and ongoing monitoring of research by independent ethical review committees.
- C. **Belmont Report:** identifies three basic ethical principles
 - (1) **Respect for Persons** requires that individuals are treated as autonomous agents and that persons with diminished autonomy are protected.
 - (2) **Beneficence** requires that the risks and benefits be managed to maximize the possible benefits and minimize the possible harms.
 - (3) **Justice** requires that the burdens and benefits be distributed equally among individuals.

Human subjects research is additionally governed by the Federal Policy for the Protection of Human Subjects (The Common Rule), codified by the Department of Veterans Affairs at Title 38 Code of Federal Regulations Part 16 (38 CFR 16). In addition, the STVHCS adheres to the Department of Health & Human Services (DHHS) regulations at 45 CFR 46 and Food & Drug Administration (FDA) regulations at 21 CFR 50, 56, 312, 361 and 812 when applicable.

6. Federalwide Assurance (FWA)

The STVHCS has obtained and continues to maintain a **FWA**. This assurance is a written commitment by an institution to protect human subjects participating in research. The STVHCS utilizes the UTHSCSA IRBs and has registered its IRBs with the Office of Human Research Protections (OHRP). A listing of the currently approved FWA for STVHCS (FWA00001220) and registration numbers for UTHSCSA IRBs (IRB00000553, IRB000002691, IRB000002692) with the expiration dates can be found at: <http://www.hhs.gov/ohrp/assurances> .

7. STVHCS Human Research Protection Program (HRPP)

The STVHCS HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the Medical Center Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Assistant Chief of Clinical Research, the administrative staff of the R&D office, compliance officers, R&D committee members, the UTHSCSA IRB committee members and office staff, other committees or subcommittees addressing human subjects protection (e.g. Radiation Safety), STVHCS investigators and research staff, health and safety staff, and research pharmacy staff. The objective of this program is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The ethical conduct of research is a shared responsibility among all individuals involved in the HRPP. It requires cooperation, collaboration, and trust among the institution, investigators and their staff, the subjects who enroll in research activities, IRB members, R&D Committee members, and R&D office staff. The Principle Investigator (PI) has the primary responsibility for the conduct of the study and the protection of human subjects.

This handbook provides important guideposts to policies and procedures that are critical to understand and follow in order to ensure that ethical standards and practices are followed and human subjects are afforded maximum protection as participants in research. If at any time you observe questionable human research activities, have questions about policy or procedures or want to submit ideas for improvement, please bring them to the attention of the STVHCS R&D office.

SECTION 4: Requirements for Personnel Involved in Human Subject Research

1. VA Appointment

All individuals (e.g. principal investigators, co-investigator, and study staff) who participate in a research protocol at the STVHCS that involves human subjects must have a VA appointment. Individuals may be either compensated by VA, be appointed to work without compensation (WOC), or may be an employee assigned to VA through the Intergovernmental Personnel Act (IPA) of 1970.

2. Principal Investigator (PI)

Each protocol involving human subject research must have a designated PI. Within VA, a PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. The FDA considers a PI and an investigator to be synonymous.

Principal investigators are responsible for the oversight of their research protocols and research staff, including recruitment, selection of study participants, and study conduct. Principal investigators may appropriately delegate and assign research responsibilities to their study staff. The PI remains accountable for all research activities even when delegated to study staff and must assure that study staff has received protocol specific training and are compliant with all federal, state, and local regulations.

3. Approved Scope of Practice

All individuals who participate in research at the STVHCS that involves human subjects must have an approved Scope of Practice that specifically defines their roles and responsibilities in the research protocol. Personnel may have only the roles and responsibilities, as defined by their approved Scope of Practice, which are appropriate to their level of training, specific license, and clinical credentials.

Licensed research personnel may *not* perform or be trained to perform procedures outside of those allowed under their respective license and credentialing. If a licensed clinician wishes to perform a clinical procedure for research purposes outside the scope of their current credentialing, he/she must have the change approved through the Medical Staff Office. Unlicensed research personnel may not be trained to do procedures that require a medical license.

Non-licensed research personnel, including individuals who have an MD, DO, BSN, or MSN degree, without licensure (excluding those in an ACGME approved training program), are not allowed to perform duties that would constitute the practice of medicine, including physical examination of subjects; ordering medications or investigational agents; altering or adjusting the dose of medications or investigational agents; evaluating acute medical problems, including

adverse events; and ordering, administering, or modifying intravenous solutions or medications. Any procedures that, according to the STVHCS bylaws, would require consent of the patient in a standard (non-research) patient care setting may not be performed by non-licensed research personnel. These procedures are listed in the Bylaws and Rules of the Medical Staff of the STVHCS, Section R3.

Unlicensed research personnel (excluding those in an ACGME approved clinical training program) may not use their educational degree after their name on IRB approved consent forms or on research staff contact lists. Unlicensed research personnel may not display their educational degree (e.g. M.D. or R.N.) on a name tag in any way that would convey to a research participant or staff that he/she is a licensed practicing clinician.

The PI is responsible for ensuring each study staff member works within their approved scope of practice.

Steps for Obtaining an Approved Research Scope of Practice

- (1) The PI must complete and submit a Research Scope of Practice to the R&D office when an individual is first added to their research protocol(s).
- (2) The ACOS for R&D and the Chief of Staff will review the Research Scope of Practice and provide approval by signature if the requested roles and responsibilities are appropriate.
- (3) The R&D office will provide the investigator and employee with a copy of the approved Scope of Practice or notification of disapproval if the Scope could not be approved as submitted.
- (4) Once approved the new/revised scope will be entered into the employee's file and tracked for review and update with each new protocol submission and/or continuing protocol review.
- (5) Investigators should retain a copy of the employee's Research Scope of Practice. A revised Research Scope of Practice must be submitted if modifications are needed to cover any changes.

4. Annual Training Requirements

All individuals who intervene or interact with research subjects or obtain private, identifiable information must complete annual human research subjects training as per VA policy and regulations. This includes individuals engaged in either exempt or non-exempt human research.

A. Collaborative Institutional Training Initiative (CITI)

CITI is a comprehensive educational program designed to provide necessary information about protecting research participants. There are two programs:

- (1) Basic Course (CITI VA GRP/GCP Course) is a comprehensive course addressing Good Clinical Practice and ethical principles of human research protection. This course should be completed first.
- (2) Continuing Education Course (Refresher Course) is designed for learners who previously completed the CITI VA GRP/GCP Course and need to meet the one-year recertification requirement.

The required modules are available on the CITI website: <http://www.citiprogram.org/>. A learner's page is created to track your training following registration on the site. Complete all the required modules listed on your learner's page. In some cases, the IRB will direct you to complete additional modules based on the type of research you are conducting (special populations, unique topics). This is determined on a protocol-by-protocol basis. A listing of these additional modules is located on the learner's page under "Optional Modules". You may complete any or all of these modules to supplement your understanding of human research ethics and regulations. There is no limit on the number of times you may use the website or view the modules. You are encouraged to bookmark the website and use the information as a reference. A passing score is 70%. If less than a passing score is obtained for a training module, the failed training modules will be reset to allow you to retake only those modules.

When you complete all of the required modules, you will be able to generate a "Completion Report" on the CITI site. In addition, CITI keeps a record of your progress that you can access any time you log on, this information is also available to the VA R&D and UTHSCSA IRB offices. When you complete the training, CITI notifies these offices electronically.

Training must be completed before any investigator or study staff can commence any human subject research and must be completed annually to continue working on active research protocols

B. VA Data Security Training

Investigators must complete training required by the VA (independent of research) to maintain their VA appointment. This is monitored and verified by the service to which the individual is appointed on an ongoing basis. Each person who has an appointment for research purposes is required to take the following training modules:

- (1) VA Research Data Security and Privacy
- (2) VA Cyber Security Awareness
- (3) VHA Privacy Policy Web Training

Training modules are available at:

<http://www.lms.va.gov/plateau/user/login.jsp> (For VA Employees)

<http://www.vcampus.com/vcekpvalo/> (For WOC Employees)

Login Instructions are available at:
<http://www.research.va.gov/programs/pride/training/docs/data-security-031507.pdf>

5. Principal Investigators Statement of Commitment and Understanding

Principal Investigators must understand their obligation to protect the rights and welfare of research subjects. The PI must ensure the presence of all necessary resources to protect research participants before conducting any research study. The following highlights continuing responsibilities of the Principal Investigator in the conduct of VA research. While this list is comprehensive it is not all inclusive and the principal investigator is encouraged to consult the STVHCS R&D Office, the UTHSCSA IRB Office, and other sources for additional information regarding Federal, State, and Institutional requirements.

- (1) Ensuring that the research protocol has sound design, minimizing risks to subjects while maximizing research benefits. Non-research procedures and data should be used to avoid adding risk or inconvenience to the subject when possible.
- (2) Conducting the study in such a way as to protect the rights and welfare of human subjects, in accordance with the principles, standards, and requirements set forth in the *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, U.S. Department of Health and Human Services regulations, and any other applicable National, State, or Institutional laws or regulations.
- (3) Conducting the study and enrolling subjects in accordance with the IRB and R&D approved current protocol and making changes to the protocol only with approval of the sponsor (if any), IRB, and R&D Committee, except in emergent situations when the changes are necessary to protect the safety, rights or welfare of subjects.
- (4) Ensuring that research subjects are fully informed of the investigational purpose of the study and the potential risks, and that all requirements relating to the adequacy of both the informed consent document and the informed consent process, including its documentation, are met.
- (5) Exercising effective oversight of all activities related to the protocol and ensuring that all research personnel involved in the conduct of the study are informed about their responsibilities, have been appropriately trained, and work within their approved Scope of Practice.
- (6) Ensuring appropriate data safety and monitoring for the protocol, monitoring of subjects for potential harm, promptly modifying the research design to mitigate any potential risks, and reporting any changes in the risk-benefit ratio to the IRB.
- (7) Ensuring that resources are adequate to effectively and safely perform the research as described in the protocol.
- (8) Reporting to the sponsor and the IRB any unanticipated problems involving risk to subjects or others (UPIRSO) that occur in the course of the research as defined by and in compliance with the IRB UPIRSO policy
([http://research.uthscsa.edu/irb/policy/UPIRSO Policy and Procedure.doc](http://research.uthscsa.edu/irb/policy/UPIRSO%20Policy%20and%20Procedure.doc).)
- (9) Maintaining appropriate documentation (enrollment, research progress, and termination notes) in the subject's electronic medical record.

- (10) Maintaining adequate and accurate source documentation and regulatory records in accordance with the Sponsor's regulations and GCP. Records must be properly secured and available for inspection in accordance with applicable National and Institutional regulations.
- (11) Ensuring that VHA and STVHCS pharmacy regulations are followed if the study involves any test article, including that a drug or device has an IND or IDE or meets criteria for exemption. Conducting research involving FDA-regulated products in compliance with all applicable FDA regulations, and fulfilling all FDA-directed investigator (or Investigator-Sponsor) responsibilities (including maintaining an accurate FDA 1572 form when appropriate).
- (12) Ensuring that the privacy and personal information of research subjects and research data is protected and disclosures are accounted for according to VA, Federal, State, and Institutional regulations.
- (13) Ensuring timely submission of information to the IRB, R&D Committee, and Compliance Office so that effective oversight of the research is maintained.
- (14) Providing the R&D Office with all STVHCS Report of Clinical Research Monitoring Visit forms from all external study monitoring visits.
- (15) Disclosing any financial Conflict of Interest relevant to the study to the STVHCS Financial Conflict of Interest Administrator and the IRB.
- (16) Ensuring that recruitment of subjects is performed in a fair and equitable manner and in accordance with all IRB, STVHCS, VHA, and other federal regulations.
- (17) Reporting any concerns, complaints, allegations of research improprieties, or research misconduct to the R&D office, who will assure communication to the appropriate component of the HRPP.
- (18) Responding to participants' questions, concerns, and complaints in an efficient and appropriate manner.

SECTION 5: Human Subjects Recruitment and Enrollment

1. Enrollment of STVHCS Veteran Patients in VA Research

Veteran patients can be enrolled in studies that:

- A. Have been approved by the UTHSCSA IRB and VA R&D committee
- B. Are performed by research investigators (VA salaried or WOC) who have completed VA credentialing and training
- C. Will be performed on-site at the VA (GCRC or other clinic)

2. Enrollment of STVHCS Veteran Patients in Non-VA Research

Veteran patients cannot be enrolled in studies performed off-site at a non-VA institution through formal referral from VA staff or through formal recruitment at the STVHCS.

- A. Active recruitment of VA patients into non-VA studies through posting of fliers at the VA is not allowed.
- B. Veteran patients have a right to seek care from and enroll in a research study outside the VA. When treatment options or relevant research studies are only available through non-VA institutions, a VA physician may inform the veteran about options outside the VA.
- C. Informing the veteran patient of the availability of an outside research study, (i.e. at the UTHSCSA) is not considered a referral, if the referring physician will not have an ongoing participation in the care of the patient.
 - (1) In informing the veteran patient about an off-site study, it should be made clear to the veteran that the VA will not be responsible for any costs related to their care at the off-site institution or their participation in the off-site research study.
 - (2) Enrollment of a veteran in a non-VA study should occur through the veteran's own initiative in contacting the study personnel at the outside institution.
 - (3) If a veteran enrolls in a research study at a non-VA institution on their own initiative the research subject should sign the consent form appropriate for that institution.
 - (4) The provision of information to a VA patient regarding potential research study options outside the VA and the patient's responsibility for any costs related to the study, should be documented by the VA physician in a progress note in the patient's electronic medical record (CPRS).
 - (5) Veterans who seek care from, or elect to enroll in a research study, at an institution outside of the VA will have access to general care (unrelated to the research study) at the VA as determined by their eligibility status.

- (6) In accordance with VHA privacy laws, VA records may not be accessed to obtain information for research purposes for a veteran research subject enrolled in a non-VA study.

3. Enrollment of Non-Veterans in VA-approved Research

Non-veterans may be entered into VA-approved research studies when there are insufficient veterans available to complete the study. All regulations pertaining to the participation of veterans as research subjects including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

4. Enrollment of STVHCS Staff in VA-approved Research

The professional and support staff of the STVHCS may be included in a research study. Special permissions must be obtained for staff to participate during their work hours, and care must be taken to ensure that participation in a study is voluntary and does not influence their employment performance or standing.

5. Enrollment of Special Populations

A. Research involving children requires the following:

- (1) A waiver granted by the Chief Research and Development Officer
- (2) Must present no greater than minimal risk
- (3) Meets all requirements of Subpart D of the DHHS or FDA regulations
- (4) VA Medical Center Director has certified that the facility is able to respond to pediatric emergencies

B. Research involving pregnant women requires the following:

- (1) Adequate provisions to monitor the risks to the participant and the fetus
- (2) Adequate consideration is given to the manner in which prospective participants are going to be selected
- (3) Adequate provision is made to monitor the actual consent process by procedures such as overseeing the process by which individual consents are secured

6. Research Populations and Situations Which are NOT Conducted at the STVHCS

- A.** Research involving fetuses (in-utero or ex-utero)
- B.** Research involving in-vitro fertilization
- C.** Research involving prisoners unless a waiver has been granted by the Chief Research and Development Officer
- D.** Research including non-veterans when there are sufficient veterans available to complete the study
- E.** Planned emergency research

7. Recruitment of Research Subjects

Recruitment may be accomplished through IRB-approved mechanisms such as physician referral or posting of IRB-approved advertisements. For additional guidance on IRB-approved recruitment mechanisms refer to the IRB policy titled “Privacy and Confidentiality During Identification and Recruitment of Research Subjects”.

It is the PI’s responsibility to assure research subjects are recruited in a fair and equitable way.

Advertisement fliers at the STVHCS must be:

- (1) Approved and stamped by the UTHSCSA IRB
- (2) Verified and stamped by the STVHCS R&D office
- (3) Approved and stamped by STVHCS Public Affairs Office

8. Preparatory to Research Activities

Review of individually-identifiable information by a VA investigator to prepare a research protocol (e.g. to generate a hypothesis, determine the feasibility to conduct a study, determine the number of eligible patients) does not require IRB or R&D approval.

In the VA, using individually-identifiable information to contact potential research subjects as part of recruitment into a research protocol is NOT considered “preparatory to research”. VA regulations differ from those described in the HIPAA Privacy Rule in this regard. An IRB approved waiver of authorization and waiver of informed consent would be required to use individually-identifiable information to contact potential research subjects. Since the VA considers recruitment part of the research protocol, IRB and R&D approval would also be required.

Pilot studies are NOT considered part of the activities “preparatory to research” and IRB and R&D Committee review and approvals would be required.

9. Researcher Contacts with Veterans

Initial contact by researchers and study staff must be in person and/or by letter. The initial contact must provide a telephone number (R&D office at 210-617-5123 or IRB office at 210-567-2351) or other means that potential subjects can use to verify the validity of the study. Research personnel must restrict telephone and other contacts with veterans to only those procedures and data elements outlined in the IRB and the R&D approved protocol. In these contacts, research personnel must not request sensitive information (i.e., social security numbers). After recruitment and during the follow-up, research personnel should begin calls by referring to previous contacts and the information provided on the informed consent document.

10. Payment for Research Subjects

Subjects are prohibited from receiving payment if the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual medical care. Payments to subjects may be permitted, with IRB approval, in the following circumstances:

- A. No direct subject benefit. The study is not directly intended to enhance the diagnosis or treatment of the medical condition for which the subject is being treated, and when the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.
- B. Others being paid. In multi-site studies, when subjects at a collaborating non-VA institution are being paid for the same participation in the same study at the same rate proposed.
- C. Comparable situations. In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.
- D. Transportation expenses. When transportation expenses are incurred by the subject that would not be incurred in the normal course of receiving treatment and which are not reimbursed by any other mechanism.
- E. The IRB must be able to verify the following in order to approve payment of subjects for a specific protocol:
 - (1) Proposed payments are reasonable and commensurate with the expected contributions of the subject.
 - (2) Terms of the subject participation and the amount of payment are listed in the informed consent document.
 - (3) Subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in, the research study; and that the payments do not constitute (or appear to constitute) coercion to participate in, or continue to participate in, the research study
- F. All patient compensations must be approved by the UTHSCSA IRB and the R&D Committee.

SECTION 6: The Informed Consent Process

Informed consent is more than just a signature on a form; it is a process of information exchange that may include, in addition to reading and signing the informed consent document, subject recruitment materials, verbal instructions, question/answer sessions and measures of subject understanding. Thus, rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the subject. The IRB, R&D Committee, clinical investigators, and research sponsors all share responsibility for ensuring that the informed consent process is adequate.

It is imperative that the PI understands and assumes the responsibility of the informed consent process for each research subject, before that subject participates in the research study. The PI remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research.

The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language must be written in "lay language", (e.g. understandable to the people being asked to participate).

1. The Informed Consent Document

The informed consent document must include but is not limited to the following:

- A. Description of the overall experience that will be encountered.** Explain the research activity and how it is experimental. Inform the human subjects of the reasonably foreseeable harms, discomforts, inconvenience and risks that are associated with the research activity. If additional risks are identified during the course of the research, the consent process and documentation will require revisions to inform subjects as they are re-contacted or newly contacted.
- B. Description of the benefits that subjects may reasonably expect to encounter.** There may be none other than a sense of helping the public at large. If payment is given to defray the incurred expense for participation, it must not be coercive in amount or method of distribution.
- C. Description of any alternatives to participating in the research project.** For example, in drug studies the medication(s) may be available through their family doctor or clinic without the need to volunteer for the research activity.
- D. Description of the extent to which personally identifiable private information will be held in confidence.** For example, some studies require disclosure of information to other parties. Some studies inherently are in need of a Certificate of Confidentiality which protects the investigator from involuntary release (e.g., subpoena) of the names or other identifying characteristics of research subjects. The IRB will determine the level of adequate requirements for confidentiality in light of its mandate to ensure minimization of risk and determination that the residual risks warrant involvement of subjects.

- E. An explanation of whatever voluntary compensation and treatment will be provided as the result of research-related injury.** Note that the regulations do not limit injury to "physical injury", but also includes psychological, social, or financial.
- F. Regulations prohibit waiving or appearing to waive any legal rights of subjects.** Subjects should not be given the impression that they have agreed to and are without recourse to seek satisfaction beyond the institution's voluntarily chosen limits.
- G. Contact persons who would be knowledgeable to answer questions of subjects about the research, rights as a research subject, and research-related injuries. These three areas must be explicitly stated and addressed in the consent process and documentation.** Twenty-four hour contact information for investigators and study staff must be made available to all research subjects within the informed consent document. The contact number for the IRB must be included in the informed consent document to answer questions about the rights of research subjects.
- H. A statement regarding voluntary participation and the right to withdraw at any time.** It is important not to overlook the need to point out that no penalty or loss of benefits will occur as a result of either not participating or withdrawing at any time. It is equally important to alert potential subjects to any foreseeable consequences to them should they unilaterally withdraw while dependent on some intervention to maintain normal function.
- I. Additional VA specific elements are required.** VA Form 10-1086, Research Consent Form, must be used as the informed consent document, and all required elements must be included. Refer to the UTHSCSA IRB website for the most up-to-date STVHCS VA informed consent template.

2. Informed Consent of Decisionally-Impaired Subjects

Research involving subjects who are mentally ill or subjects with impaired decision-making capacity warrants special attention. Research involving these populations frequently presents greater than minimal risk; may not offer direct medical benefit to the subject; and may include a research design that calls for washout, placebo, or symptom provocation. In addition, these populations are considered to be vulnerable to coercion.

Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

- A.** Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.
- B.** The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless

that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

- C. Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC)) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.
- D. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.
- E. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.
- F. The PI may obtain consent by a legally authorized representative only in situations where the prospective subject is incompetent or has impaired decision-making capacity, as determined and documented in the person's medical record in a signed and dated progress note. The determination that a subject is incompetent or has an impaired decision-making capacity must be made by a legal determination or a determination by the practitioner, in consultation with the chief of service after appropriate medical evaluation that the prospective subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time.
- G. In cases where the determination that a prospective subject lacks decision-making capacity is based on a diagnosis of mental illness, VA policy requires consultation with a psychiatrist or licensed psychologist.

3. Legally Authorized Representatives

A legally authorized representative of a subject can provide consent for a patient with impaired decision-making capacity (surrogate consent). Texas State law differs slightly from VA regulations pertaining to the definition of Legally Authorized Representative for surrogate consent.

- A. Both VA and Texas have laws concerning general informed consent (see 38 CFR 17.32 as implemented by VHA Handbook 1044.1 and Texas Health and Safety Code Chapter 313).
- B. VA has specific federal administrative law concerning surrogate consent for participation in VA approved research studies; Texas has no such specific law. Texas general law addresses surrogate consent, but not in the research context.
- C. In matters of the interpretation of law, both statutory and administrative, the specific controls over the general, therefore STVHCS follows VA regulations pertaining to who can provide surrogate consent.
- D. VHA Handbook 1200.5 Section 11a(2), implementing 38 CFR 116.116, establishes the only surrogate entities in the following order of priority who are allowed to provide consent for research purposes at the STVHCS.

- (1) Health care agent appointed by the person in a durable power of attorney for health care (DPAHC) or similar document
 - (2) Court-appointed guardians of the person
 - (3) Next-of-kin in the following order of priority: spouse, adult child (18 years or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older).
- E. Texas law allows other individuals (close friend or member of the clergy), but the more specific VA regulation would exclude these individuals from providing surrogate consent.
- F. Texas law specifically prohibits surrogate consent for electroconvulsive therapy (ECT). VA regulations are silent regarding surrogate consent for ECT, therefore STVHCS would follow the specific Texas law in this situation.
- G. Where there is a question of interpretation of applicability of State law, the Regional Counsel for the STVHCS is consulted.

SECTION 7: Documentation of Human Subjects Research in the Patient's Health Record

1. Research Documentation in the Legal Medical Record

It is mandatory that information be listed for all research studies that have been determined to be more than minimal risk to inform other investigators and clinicians that a veteran is enrolled in a research study. The PI is responsible to ensure that documentation of research enrollment and activities is made in the patient's legal health record. A patient's legal health record includes the electronic medical record (CPRS) and any additional hard copy documents located in Medical Records. Research files maintained by the PI and/or research staff are not part of the legal health record. **Investigators failing to comply with this mandatory requirement will face loss of research privileges.**

2. Documentation of the Informed Consent Process

The informed consent process must be documented by the use of an IRB-approved written consent form on VA Form 10-1086 (Informed Consent Document). It must be signed by (a) the participant or the participant's legally authorized representative, (b) a witness, and (c) the person obtaining the informed consent, unless an IRB consent waiver has been approved. The consent document must be stamped with the date of the most recent IRB approval. A copy of all signed research informed consents must be placed into the participant's health record. Investigators are to keep the original signed copy of the informed consent in the participant's research record.

A. Documentation of Enrollment: When a VA patient signs an informed consent document and is enrolled in a VA study, a research note must be entered using the "Research Enrollment/Consent Note" template located in CPRS. The following information is included in the note:

- (1) Name of the study
- (2) Name of the principal investigator
- (3) IRB protocol number
- (4) Name of the person obtaining the participant's consent
- (5) Name of the participant's legally-authorized representative if applicable
- (6) A statement that the study/consent process was explained to the participant, or the participant's legally-authorized representative
- (7) A statement that the participant, or the participant's legally-authorized representative, expressed an understanding the study
- (8) A statement that the participant, or the participant's legally-authorized representative, was given the opportunity to ask questions
- (9) A statement that the participant, or the participant's legally-authorized representative, was given a copy of the consent form
- (10) A statement that the research protocol does or does not involve the administration of medications, drugs, or experimental substances
- (11) Contact information for a member of the research team that is available at all times and from whom additional information concerning the study can be obtained

- B. Flagging the Participant's Health Record:** The “Research Enrollment/Consent Note” template must be used to flag the participant’s medical record in CPRS. The note will be in the postings (CWAD- Crisis notes, Warning notes, Advanced Directives) indicating the patient is enrolled in a research study.

Vista CPRS in use by: Summers, Kimberly (mirrorserver.san-antonio.med.va.gov)

File Edit View Action Options Tools Help

AA-BELNU, NLENL LKR ISCPHA Jan 08, 08 11:35 Primary Care Team Unassigned

101-17-9189 Feb 27, 1950 [57] Provider: SUMMERS, KIMBERLY

Flag Remote Data? ? Postings W

Visit: 01/08/08 RESEARCH CONSENT/UPDATE NOTE, ISC PHARM D, KIMBERLY SUMMERS (Jan 14, 08@13:39)

LOCAL TITLE: RESEARCH CONSENT/UPDATE NOTE
DATE OF NOTE: JAN 14, 2008@13:39 ENTRY DATE: JAN 14, 2008@13:39:30
AUTHOR: SUMMERS, KIMBERLY EXP COSIGNER:

Patient Postings

Allergies Severity Signs / Symptoms

No Allergy Assessment

Crisis Notes, Warning Notes, Directives

Research Consent/Update Note	Jan 14, 08
Research Disenrollment/Termination Note	Jan 11, 08
Research Consent/Enrollment Note	Jan 08, 08
Research Disenrollment/Termination Note	Jan 08, 08
Research Consent/Enrollment Note	Nov 06, 07

Close

*****ONLY AUTHORIZED RESEARCH PERSONNEL*****

/es/ KIMBERLY SUMMERS
PharmD ISC
Signed: 01/14/2008 13:40

NEW PATIENT Brief Exam
Diagnoses: Cerebellar or brain stem laceration with open intracranial wound, with state of (Primary)

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

start Inbox - Microsoft Out... Microsoft PowerPoint... CPRS - Patient Chart 1:40 PM

C. Electronic Scanning of Documents

The Research Pharmacy will not dispense any study medications for a research subject until all 10-1086 (VA consent form) and 10-9012 (Investigational Drug Information Record) forms have been scanned in the subject’s medical record.

(1) Informed Consent Documents

A copy of the signed and dated VA consent form (VA Form 10-1086) must be submitted to the Medical Records office for scanning and electronic attachment to the “Research Consent/Enrollment Note”.

(2) Investigational Drug Information Record

If the study protocol involves the administration of medications, drugs, or experimental substances, a copy of the completed and signed Investigational Drug

Information Record(s) (VA Form 10-9012) must be submitted to the Medical Records office for scanning and electronic attachment to the “Research Consent/Enrollment Note”. Attachment of VA Form 10-9012 will provide documentation of information on possible drug interactions and adverse effects of investigational drugs being administered in the patient’s health record.

(3) Scanning Procedures

Documents will be scanned within 24 hours of completion of the CPRS note template and delivery to the Medical Records Department. The CPRS note templates must be signed prior to scanning. Submit good quality, dark copies for scanning. Assure there are no pages missing from the informed consent document. Assure there are patient identifiers on all pages (**NOTE: on the 10-9012 there is no specified placed for patient identifiers you must write them in**).

a. Faxing Documents

Copies of documents can be faxed to **(210) 949-3373**.

b. Stat Scanning

If scanning is required immediately for the dispensing of medication on the same day as signing of informed consent contact:

Anthony Salvagno at ext 16067 or Rey Flores at ext 15605

Scanning will be completed within 15 minutes. **Please do not abuse this system**. This procedure is only for situations where dispensing of medications in less than 24 hours of initial consenting is required.

c. Scanning After Hours

Medical Records Department hours: 7:00am to 12:00am Monday thru Friday. After hours, fax documents to Medical Records Department at (210) 949-3373 for scanning the next business morning.

D. Documentation of an Updated Research Consent

Any changes to the research protocol resulting in an addendum or updated informed consent document must be entered into the subject’s health record. After a patient signs the addendum or update, a research study note must be entered using the “Research Consent/Update Note” template located in CPRS. A copy of the signed and dated VA consent form addendum or updated informed consent must be submitted to the Medical Records office for scanning and electronic attachment to the “Research Consent/Update Note”. The “Research Consent/Update Note” template must be used to flag the participant’s medical record in the CPRS. The note will be in the postings (CWAD- Crisis notes, Warning notes, Advanced Directives) indicating the patient has been informed of new information regarding the research study.

3. Documentation of Research Visits

Any research information, which has the potential to impact the medical care of the participant, must be entered into the medical record (CPRS). A “Research Progress Note” must be entered to provide the following relevant information to providers participating in the care of that patient:

- A. Any research procedures or interventions that may impact a patient’s clinical care, including the indications and potential risks of physical or psychological adverse events.
- B. Any results, including laboratory studies, physical exam findings, or medical interventions, from the research that is relevant to the medical care of the participant.
- C. Any information regarding possible drug interactions and/or toxicity of the pharmaceutical agents administered as part of the research protocol.
- D. All progress note titles are standardized to start with “Research”.
- E. A research progress note is not required for the following:
 - (1) Case report forms
 - (2) Surveys
 - (3) Questionnaires
 - (4) One time visits AND no additional PHI is collected after the one time visit AND no information collected would benefit another provider

Documentation of assessments and procedures in the progress note must fit with the provider’s approved Scope of Practice.

4. Documentation of Disenrollment or Termination from a Research Study

When a participant is disenrolled or terminated from a research protocol, a research study note must be entered using the “Research Disenrollment/Termination Note” template located in CPRS. The following information is included in the note:

- A. Name of the study
- B. Date of disenrollment or termination
- C. Contact information for a member of the research team from whom additional information concerning the study can be obtained

5. Flagging of the Medical Record Waived by IRB

When the IRB determines that flagging the medical record and scanning the informed consent document would increase the subject’s risk or compromise the study results, flagging the record and documentation in the subject’s health record will be waived. The IRB approval letter must state the flagging requirement has been waived to protect the subject or study integrity. The

investigator will be notified of the approval to waive the flagging requirement in the R&D protocol approval letter.

6. Questions Regarding CPRS Documentation

If you have any questions about progress note documentation or require training on how to use CPRS, please contact the STVHCS CPRS Clinical Coordinators at (210) 617-5300 ext 15519.

SECTION 8: The Handling of Investigational Drugs for STVHCS Research Studies

1. The VA Research Pharmacy

The Research Pharmacy will assist investigators in conducting clinical research. The research pharmacy is involved in all phases of investigational drug studies, from planning through completion. It is required, with only rare exceptions that all investigational medications go through the STVHCS Research Pharmacy. Under special circumstances, the Research Pharmacy may delegate in writing the custody of investigational drugs stored outside the pharmacy to the PI (see Section 8 Number 12: Delegation of Custody of Investigational Drugs Stored Outside the Pharmacy).

A. Research Pharmacy Contact Information

		VA Ext	Pager
George Melnik, PharmD	Research Pharmacy Manager	(210)617-5300x14463	(210)203-9291
Virginia Doyal, PharmD	Protocol Pharmacist	(210)617-5300x16984	(210)205-9940
Rebecca Greene, PharmD	Oncology Pharmacist	(210)617-5300x14527	(210)203-2302

B. Services Provided by the Research Pharmacy Include:

- (1) Meeting with company sponsors for protocol review and pharmacy procedures
- (2) Ordering and handling shipments of investigational drugs
- (3) Compounding support for double blind studies
- (4) Patient randomizations schedules for study protocols
- (5) Record keeping for investigational drugs (dispensing, inventory control)
- (6) Assistance with completion of the Drug Information Sheet (VA Form 10-9012)
- (7) All Pharmacy investigational drug requirements to meet medical center policies
- (8) For other specialized services consult the Research Pharmacist

C. Approval of Protocols Involving Investigational Drugs

Investigational protocols must have the approval of the R&D committee and the IRB prior to the ordering, receipt, storage, or dispensing of investigational drugs.

The R&D Committee cannot approve a proposal involving investigational drugs unless the Chief of Pharmacy Service documents in writing that pharmacy resources are adequate or that satisfactory provisions have been made to reimburse pharmacy for the services provided. The principle investigator must complete a “Statement of Clinical Research Impact on VA Hospital Services” which is forwarded to the Research Pharmacy Manager for review and signature by the Chief of Pharmacy Services.

Documentation Required by the Research Pharmacist

For each approved protocol, the PI is responsible for ensuring the Research Pharmacist has the following documents:

1. Approval letter signed by the R&D Chairperson
2. Approval letter signed by the IRB Chairperson, or VA Form 10-1223, Report of Subcommittee on Human Studies, signed by the IRB director
3. A copy of VA Form 10-9012 (Investigational Drug Record) when appropriate
4. A copy of the approved protocol
5. A copy of the most recent IRB approved informed consent (IRB stamped VA Form 10-1086)
6. Documentation of each continuing review process
7. Notice of termination for clinical investigations involving investigational drugs

D. The Research Pharmacy and The Human Research Protection Program (HRPP)

The handling of investigational drugs given to VA patients must optimize patient safety and satisfy the requirements of the governing VA policy and regulations. The Research Pharmacy is responsible for implementation and monitoring of HRPP requirements associated with the use of investigational drugs and devices.

2. Definition of Investigational Drug

An investigational drug is a chemical or biological drug that is used in a clinical investigation. An investigational drug can be:

- A. A new chemical compound, which has not been released by the Food and Drug Administration (FDA) for general use
- B. An approved drug that is being studied for an approved or unapproved use, dose, dosage form, administration schedule, or under an Investigational New Drug (IND) application, in a controlled, randomized, or blinded clinical trial
- C. Concurrent medications, comparators, or rescue medications used in the investigational trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels.

3. Receipt and Storage of Investigational Drugs by the Research Pharmacy

Regardless of the source, all investigational drugs must be delivered to the Research Pharmacy for receipt, storage, security, dispensing, distribution, and disposition. Distribution to other locations such as Community Based Outpatient Clinics (CBOC) or University Hospital (UH) occurs from the STVHCS Research Pharmacy. A letter of understanding (LOU) must be in place to transfer investigational medications to another facility.

The Research Pharmacist is responsible for and will maintain a log of all transactions involving receipt, storage, security, dispensing, and disposition of unused investigational drugs. All investigational drugs will be:

- A. Secured in the pharmacy

- B. Stored separately from the non-investigational drugs
- C. Be clearly identified as investigational

The Research Pharmacist will maintain a drug log with the following information for each investigational drug:

1. Name of the drug, dosage form, and strength
2. Manufacturer or other source
3. Date of receipt of the drug
4. Quantity received
5. Expiration, retest, or repass date
6. Control, lot number, or other identification (ID) number
7. Name of site investigator
8. Protocol name or number
9. Name of subject or other subject identifier for individuals receiving the medication
10. Verification of a signed and dated informed consent document for the subject
11. Quantity dispensed
12. Balance of drug currently available
13. Recorder's initials
14. Serial number of the subject and date the investigational drug was dispensed
15. A final entry is made when drug therapy for the entire study (at the site) has ended

4. Dispensing of Investigational Drugs by the Research Pharmacy

Investigational drugs may be dispensed only by order or prescription from an authorized investigator (the investigator must be listed on the VA Form 10-9012). All prescriptions must contain the following information:

1. Date
2. Provider's signature
3. Participant's name
4. Identification number (study number and last 4 of social security number)
5. Quantity prescribed
6. Complete directions for use

In addition to the generally required prescription label information and appropriate auxiliary caution or warning labels, all investigational drug labels will also include the following legend: "CAUTION – NEW DRUG: LIMITED BY FEDERAL LAW TO INVESTIGATIONAL USE".

5. Ordering of Investigational Drugs in CPRS

Providers are encouraged to enter orders into CPRS for investigational medications. Use "Investigational ..." for outpatient RX entering. Provide the following information in the comments section:

1. Name of study drug
2. Participant's study number
3. Protocol abbreviation

The Research Pharmacist also currently accepts handwritten and faxed prescriptions.

A. Verifications by the Research Pharmacist Prior to Dispensing

The research pharmacist will verify that the Informed Consent document (VA Form 10-1086) has been signed, dated, and scanned into CPRS through Vista Imaging for each participant. The research pharmacist will document review of the signed informed consent in the investigational drug file. The research pharmacist will also verify that the Investigational Drug Information Form (VA Form 10-9012) has been scanned into CPRS through Vista Imaging for each participant.

B. Release of Filled Investigational Drug Orders

Investigational drugs will be dispensed directly to the patient, agent of the patient, or to study personnel. Investigational drugs can be picked up at the Research Pharmacy located in room K038 in the basement of the STVHCS.

C. Patient Co-pays

VA medication co-payments will be waived if the medication is provided to the patient as part of a VA-approved research protocol. This is true even when the sponsor of the investigational study does not provide the medication. Co-payment eligible patients, participating in VA-approved research projects should not be charged for inpatient or outpatient medications provided through an investigational drug study. Co-payment eligible patients are still subject to appropriate co-payments for VA provided medications for non-research medical care.

6. VA Research Pharmacy Charges

All investigators must submit information to the STVHCS Research Pharmacy to allow for the calculation of the pharmacy costs for each new investigational drug protocol.

All investigational drugs and supplies must be provided by the study sponsor. When commercially available medications are part of the investigational drugs and the sponsor does not provide them and medical care appropriations are utilized for their purchase, that amount must be reimbursed from the research appropriations. Concurrent, comparator, or rescue medications that are required by the study sponsor and used for study-related purposes will be recorded by the dispensing pharmacy as part of the study treatment. When the sponsor does not provide these medications and medical care appropriations are utilized for their purchase, that amount must be reimbursed from the research appropriations.

7. Investigational New Drug Application (IND)

An Investigational New Drug Application (IND) is a request for Food and Drug Administration (FDA) authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application. If a project sponsor has not obtained an IND or the PI is the project sponsor, it is the responsibility of the PI to obtain an IND or provide documentation that the project meets criteria for exemption.

IND regulations are contained in CFR 21, Part 312. Application forms for submission of an IND and additional information can be obtained at the following website:

<http://www.fda.gov/cder/forms/1571-1572-help.html>.

FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.

A. Determining if Your Protocol Requires an IND

- (1) Research involving the administration of any investigational drug to humans requires submission of an IND
- (2) Research involving the administration of an approved drug for an unapproved use, where the choice of drug, dose, timing or route is dictated by the study requires submission of an IND if any of the following are applicable:
 - a. The investigation is intended to be reported to the FDA to support a new indication for use of the drug or intended to be used to support any other significant change in the labeling of the drug
 - b. The investigation is intended to be reported to the FDA to support a significant change in the advertising of the drug
 - c. The investigation involves a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug
- (3) An IND is not required for investigations which meet one of the 5 exemptions under 21 CFR 312.2(b)

For additional guidance and information refer to the UTHSCSA IRB website:

<http://research.uthscsa.edu/irb/> Form O-1.

B. Principle Investigator as the Project Sponsor (Sponsor-Investigator)

A Sponsor-Investigator is an individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug is being administered or dispensed. **NOTE: If a pharmaceutical company will be supplying the drug, but will not itself be submitting the IND, the company is not the sponsor.**

When an investigator files an IND, the investigator is considered the sponsor and as such carries all of the FDA regulatory responsibilities and reporting obligations of both the investigator and sponsor as outlined in the FDA regulations 21 CFR 312 and 21 CFR 601. Please refer to the regulations for complete information.

C. IND Submission

The following information is required for an IND application:

- (1) Cover sheet
- (2) Table of contents
- (3) Investigator brochure
- (4) Protocols
- (5) Chemistry, manufacturing, and control information
- (6) Pharmacology and toxicology information
- (7) Previous human experience with the investigational drug
- (8) Additional information on special topics if need (e.g. drug dependence and abuse potential, radioactive drugs, pediatric studies)
- (9) Relevant information if requested by FDA

A sponsor-investigator who uses, as a research tool, an investigational new drug that is already subject to a manufacturer's IND or marketing application may, if authorized by the manufacturer, refer to the manufacturer's IND or marketing application in providing the technical information supporting the proposed clinical investigation.

D. FDA Receipt of the IND

Upon receipt of the IND by FDA, an IND number will be assigned, and the application will be forwarded to the appropriate reviewing division. The reviewing division will send a letter to the sponsor or sponsor-investigator providing notification of the IND number assigned, date of receipt of the original application, address where future submissions to the IND should be sent, and the name and telephone number of the FDA person to whom questions about the application should be directed. Studies shall not be initiated until 30 days after the date of receipt of the IND application by FDA unless the sponsor or investigator receives earlier notification by the FDA that studies may begin.

E. Correspondence with FDA Following Approval of an IND

Protocol amendments related to an approved IND are required for:

- (1) New protocols that use the same IND
- (2) Changes in an existing protocol under the IND
- (3) Information amendments
 - a. New toxicology, chemistry, or other technical information
 - b. Discontinuation of a clinical investigation

Any adverse experience associated with the use of the drug that is both serious and unexpected during the IND period must be submitted to the FDA as an IND safety report.

The sponsor shall within 60 days of the anniversary date that the IND went into effect, submit a brief report of the progress of the investigation.

F. IRB Approval

The UTHSCSA IRB requires the IND number be provided with the initial protocol submission packet. Approval will not be granted until the IND number has been received, unless documentation is provided that the project meets criteria for exemption. Additional questions regarding the criteria for exemption for an IND should be addressed to the UTHSCSA IRB.

G. FDA Reporting Obligations for an IND

FDA reporting obligations of investigators under an IND include:

- (1) Drug disposition
- (2) Case histories
- (3) Progress reports
- (4) Safety reports
- (5) Final report
- (6) Financial disclosure report
- (7) Specific record keeping and record retention

FDA reporting obligations of sponsors under an IND include:

- (1) Protocol amendments
- (2) Information amendments
- (3) IND Safety Reports
- (4) Annual Reports
- (5) Withdrawal of an IND
- (6) Specific record keeping and retention

8. Off Label Drug Use

A physician may use a marketed drug in an unapproved manner without obtaining an IND, if it is given for therapeutic rather than investigational purposes (21 CFR ¶ 312.2[d]). Additional information regarding off label drug use is available at

<http://vaww.pbm.va.gov/directive/Guidance%20Off%20Label%20Prescribing.pdf>

9. Treatment or Protocol IND

During the clinical investigation of a drug, it may be appropriate to use the drug in the treatment of a patient who is not in the clinical trial, in accordance with a treatment protocol or treatment

IND. The FDA permits an investigational drug to be used for a treatment under a treatment protocol or treatment IND if:

1. The drug is intended to treat a serious or immediately life-threatening disease
2. There is no comparable alternative drug or other therapy available to treat that stage of the disease in the intended patient
3. The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed
4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence

Prior to the institution of treatment, a treatment protocol submitted by an IND sponsor or a treatment IND submitted by a licensed practitioner is required.

1. A licensed practitioner should first attempt to obtain the drug from the sponsor of the controlled trial under a treatment protocol.
2. If the sponsor of the controlled trial of the drug will not establish a treatment protocol for the drug in accordance with 21 CFR312.35(a), the practitioner may seek to obtain the drug from the sponsor and submit a treatment IND to FDA requesting authorization to use the investigational drug for treatment use.

Treatment under a treatment IND may begin 30 days after FDA receives the IND or on earlier notification by FDA that the treatment use under the IND may begin.

A treatment IND is required to contain the following:

1. A cover sheet (Form FDA 1571) available at <http://www.fda.gov/cder/forms/1571-1572-help.html>
2. Information (when not provided by the sponsor) on the drug's chemistry, manufacturing, and controls, and prior clinical and nonclinical experience with the drug
3. A statement of the steps taken to obtain the drug under a treatment protocol from the drug sponsor
4. Treatment protocol containing
 - a. Intended use of the drug
 - b. Explanation of the rationale for use of the drug, including, as appropriate, either a list of what available regimens ordinarily should be tried before using the investigational drug or an explanation of why the use of the investigational drug is preferable to the use of available marketed treatments
 - c. A brief description of the criteria for patient selection
 - d. The method of administration of the drug and the dosages
 - e. A description of clinical procedures, laboratory tests, or other measures to monitor the effects of the drug and to minimize risk
5. A statement of the practitioner's qualifications to use the investigational drug for the intended treatment use

6. The practitioner's statement of familiarity with information on the drug's safety and effectiveness derived from previous clinical and nonclinical experience with the drug
7. Agreement to report to FDA safety information

A licensed practitioner who submits a treatment IND is the sponsor-investigator for such IND and is responsible for meeting all applicable sponsor and investigator responsibilities under 21 CFR 312.

If a treatment IND is initiated, you are encouraged to contact the IRB Director for additional information and guidance (Joseph O. Schmelz, Ph.D., CIP at (210) 567-2357). Informed consent is required unless the conditions for exemption are met.

10. Emergency Use of an Investigational New Drug (IND)

Need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND in accordance with the above requirements (CRF 312.23 and 312.34). In such a case, FDA may authorize shipment of the drug for a specified use in advance of submission of an IND. A request for such authorization may be transmitted to FDA by telephone or other rapid communication.

1. For investigational biological drugs regulated by the Center for Biological Evaluation and Research, contact the Office of Communication, Training and Manufacturers Assistance, Center for Biologics Evaluation and Research @ 301-827-2000.
2. For all other investigational drugs, contact the Division of Drug Information, Center for Drug Evaluation and Research @ 301-827-4570
3. After normal working hours, eastern standard time, contact the FDA Office of Emergency Operations @ 301-443-1240

Emergency Exemption from Prospective IRB Approval

Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval.

Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating.

1. Life-threatening means disease or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-

- threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
2. Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

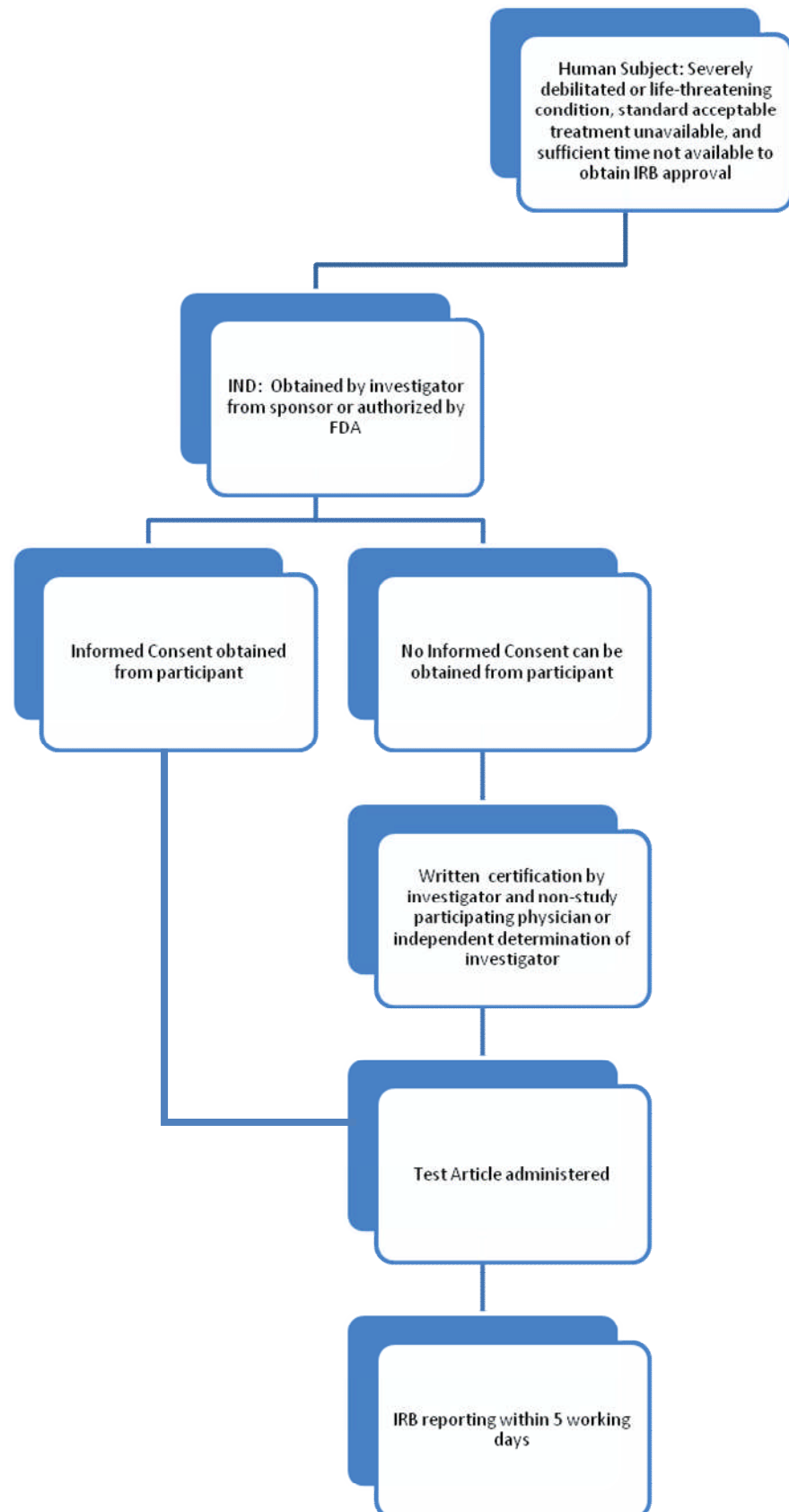
Exception From Informed Consent Requirement

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
3. Time is not sufficient to obtain consent from the subject's legal representative.
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If an emergency use of an IND is initiated, you are encouraged to contact the IRB Director for additional information and guidance (Joseph O. Schmelz, Ph.D., CIP at (210) 567-2357). Informed consent is required unless the conditions for exemption are met. An informed consent template for emergency IND use is available on the UTHSCSA IRB website at: http://research.uthscsa.edu/irb/forms_A-Z.shtml The IRB must be notified within 5-working days when an emergency exemption is used.

Emergency IND Algorithm



11. Investigational Devices

Federal law prohibits the distribution of new medical devices until the FDA has reviewed clinical data and determined the safety and effectiveness of a particular product for a specific use in human patients. An investigational device is defined as a new medical device not yet approved by the FDA that is in clinical stages of evaluation for general use and is not available for distribution through regular channels of interstate commerce.

A. Medical Device

The term "device" means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is:

- (1) Recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- (2) Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- (3) Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

An unapproved medical device is a device that is used for a purpose or condition for which the device requires, but does not have an approved application for pre-market approval under Section 515 of the Food, Drug, and Cosmetic (FD&C) Act. Medical devices that have not received marketing clearance under Section 510(k) of the FD&C Act are also considered unapproved devices.

B. Investigational Device Exemptions (IDE)

An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device. Use of an investigational device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA's IDE regulations, 21 CFR Part 812, other applicable FDA regulations, and applicable VHA regulations.

IDE regulations are contained in CFR 21, Part 812. Application forms for submission of an IDE and additional information can be obtained at the following website:

<http://www.accessdata.fda.gov>

C. Determining if Your Protocol Requires an IDE

(1) Exempt Studies

In accordance with 21 CFR 812.2(b), sponsors and investigators of certain studies are exempt from the requirements of 21 CFR Part 812. Examples of exempt studies are consumer preference testing, testing of a device modification, or testing of two or more devices in commercial distribution if the testing does not collect safety or effectiveness data, or put subjects at risk. [See 21 CFR 812.2(c) (4) for additional information]. Studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling are exempt from Part 812.

Diagnostic device studies are exempt from the requirements of 21 CFR Part 812 under certain circumstances. The study is exempt as long as the sponsor complies with the requirements of 21 CFR 809.10(c) for labeling, and if the testing:

- i. Is noninvasive
- ii. Does not require an invasive sampling procedure that presents significant risk
- iii. Does not by design or intention introduce energy into a subject
- iv. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

(2) Significant Risk Device Studies

If the study of the device is not exempt (21 CFR 812.2(c)), the device must be characterized as “significant risk” (SR) or “non-significant risk” (NSR) by the IRB. If the FDA has already made the risk determination, the IRB is not required to make the determination of SR or NSR, but will verify that a SR device has an FDA-approved IDE. A significant risk device is defined as an investigational device that is:

- i. Intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject
- ii. Purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject
- iii. For use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject
- iv. Otherwise a potential for serious risk to the health, safety, or welfare of a subject

A sponsor must submit an IDE application to FDA if a SR device is planned for use in an investigation. Sponsors and investigators of these studies must comply with the regulations at 21 CFR Part 812.

(3) Non-Significant Risk Device Studies

A NSR device is an investigational device that does not meet the definition of a significant risk device. If the IRB finds that an investigational medical device study poses a NSR, the sponsor does not need to submit an IDE to FDA. FDA considers a NSR device study to have an approved IDE after IRB approval and when the sponsor meets the abbreviated requirements at 21 CFR 812.2(b):

Abbreviated IDE: An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

- i. Labels the device in accordance with 812.5;
- ii. Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
- iii. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).
- iv. Complies with the requirements of 812.46 with respect to monitoring investigations;
- v. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);
- vi. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
- vii. Complies with the prohibitions in 812.7 against promotion and other practices.

For additional guidance and information refer to the IRB website @ <http://research.uthscsa.edu/irb/> Form O-1 and the FDA website @ <http://www.fda.gov/default.htm>

D. IDE Submission

The following information is required by the FDA for the IDE application:

- (1) Name and address of the sponsor
- (2) Complete report of prior investigations of the device and an accurate summary of those sections of the investigational plan (purpose, protocol, risk analysis, description of device, monitoring procedures, labeling, consent materials, IRB

information, other institutions, additional records and reports) or complete plan.

- (3) A description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and, where appropriate, installation of the device.
- (4) An example of the agreements to be entered into by all investigators to comply with investigator obligations under FDA rules, and a list of the names and addresses of all investigators who have signed the agreement.
- (5) A certification that all investigators who will participate in the investigation have signed the agreement, that the list of investigators includes all the investigators participating in the investigation, and that no investigators will be added to the investigation until they have signed the agreement.
- (6) A list of the name, address, and chairperson of each IRB that has been or will be asked to review the investigation and a certification of the action concerning the investigation taken by the IRB.
- (7) The name and address of any institution at which a part of the investigation may be conducted that has not been identified as in number 6 above.
- (8) If the device is to be sold, the amount to be charged and an explanation of why sale does not constitute commercialization of the device.
- (9) A claim for categorical exclusion under 21 CFR 25.3 or 25.34 or an environmental assessment under 21 CFR 25.40. (see FDA website for additional guidance if this applies)
- (10) Copies of all labeling for the device.
- (11) Copies of all forms and informational materials to be provided to subjects to obtain informed consent.
- (12) Any other relevant information if requested by FDA

E. IRB Approval

Final IRB approval will not be granted for a device study until the IDE number has been received, unless documentation is provided that the project meets criteria for an abbreviated or exempt IDE. Additional questions regarding the criteria for IRB approval of device studies should be addressed to the UTHSCSA IRB.

F. Responsibilities of the Sponsor for an IDE

Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring proper monitoring of the investigation, ensuring that IRB review and approval are obtained, submitting an IDE application to FDA, and ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation.

G. Emergency Use of an Unapproved Device

There may be circumstances under which an investigator may wish to use an unapproved device to save the life of a patient or to prevent irreversible morbidity when there exists no other alternative therapy. An investigator may treat a patient with an unapproved medical device in an emergency situation if he/she concludes that:

- (1) The patient has a life-threatening condition that needs immediate treatment
- (2) No generally acceptable alternative treatment for the condition exists; and
- (3) Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

In the event that a device is used in circumstances meeting the criteria listed above, the investigator should follow as many of the patient protection procedures listed below as possible:

- (1) Informed consent from the patient or legal representative unless criteria for exemption have been met
- (2) An assessment from a physician who is not participating in the study
- (3) Authorization from the IDE sponsor, if an IDE exists for the device
- (4) It is recommended that you contact the UTHSCSA IRB Director for additional guidance and information
- (5) Notification of the emergency use to the IRB and FDA is required within 5 working days

For investigational devices under an IDE, the IDE regulation permits deviations from the investigational plan without prior approval when necessary to protect the life or physical well-being of a subject in an emergency. [See 21 CFR 812.35(a)]

H. Investigational Medical Devices and the Research Pharmacy

The PI or a designated research staff member is responsible for delivering investigational devices to the Research Pharmacist for proper storage. The storage area for the investigational device must be separate from storage areas for approved devices. An investigational device, or its immediate package, must bear a label with the following information:

- (1) Name and place of business of the manufacturer, packer or distributor
- (2) The quantity of contents, if appropriate
- (3) A statement as follows: "CAUTION: Investigational Device. Limited by Federal law to investigational use."
- (4) Description of all relevant contraindications, hazards, adverse effects, interfering substances or devices, warning, and precautions

The Research Pharmacist will be responsible for receiving and dispensing investigational devices and will maintain a log containing the following information for each device:

(1) Upon receipt of the device:

- (a) Number of devices received
- (b) Date received
- (c) Name of the device
- (d) Serial number
- (e) Model number

(2) At the Time of Dispensing:

- (a) Name of issuer
- (b) Name of subject receiving the device
- (c) Name of the device
- (d) Serial number of the device
- (e) Number of devices left in inventory

The investigator will be responsible for coordinating with the Research Pharmacist to ensure that investigational devices are secured in a locked room or in a locked cabinet within a designated research area that is not accessible to anyone other than the Principal Investigator or their research staff.

12. Delegation of Custody of Investigational Drugs Stored Outside the Pharmacy

The Chief, Pharmacy Services, through the Research Pharmacy Manager may delegate in writing through a contractual agreement the custody of investigational drugs stored outside the pharmacy to the PI. This occurs under exceptional circumstances when an investigational drug study cannot be accomplished through the standard practice of storage and dispensing of an investigational drug from the Research Pharmacy.

The contractual agreement will specify the location for storage of the drug, the investigator responsible for the storage and dispensing of the drug, and the information that must be documented in the drug-dispensing log. The Research Pharmacy will inspect the stored drug and the drug-dispensing log on at least a monthly schedule and will notify the PI if any changes need to be made.

13. Receipt of Investigational Drugs from an Outside Institution

It is recognized that many studies involve multiple sites and the sponsor may ship the investigational drug to a non-VA pharmacy for distribution. The VA Research Pharmacy can accept transfer of investigational drugs directly from an outside pharmacy for administration to the veteran subject at the VA, provided the VA Research Pharmacy has complete information and documentation related to the drug. This transfer must be documented by memorandum from the non-VA Pharmacist to the VA research pharmacist. The VA Research Pharmacist will

document receipt of the Investigation Drug and will ensure that all the necessary drug information is on file in the VA Research Pharmacy. The following information must be on file in the VA research pharmacy prior to the dispensing of the drug by the VA research pharmacy:

- (1) A copy of the study protocol
- (2) Investigational Drug Dispensing Log
 - a. Name of the investigational drug
 - b. Manufacturer or other source of the investigational drug
 - c. Date of receipt of the investigational drug
 - d. Quantity of investigational drug received
 - e. Expiration date of investigational drug
 - f. Control number of investigational drug
 - g. Date protocol approved by VA R&D
 - h. Name of authorized practitioner signing the order or prescription
 - i. Name of patient receiving the prescribed investigational drug
 - j. Serial number of the prescription
 - k. Quantity of investigational drug dispensed
 - l. Balance of investigational drug remaining after transaction
- (3) Investigational Drug Information Record, (VA Form 10-9012)
- (4) A copy of each signed VA patient consent form, (VA Form 10-1086)
- (5) Receipts for medication from the manufacturer
- (6) General information on the drug
- (7) Dispensing instructions
- (8) The location for storage of the drug

SECTION 9: Protocol Development and Submission for R&D Approval

1. Required Protocol Elements

Research protocols submitted to the R&D Committee must be of sound scientific design. At a minimum each research protocol must include the following:

- (1) Study problem
- (2) Relevance of the project
- (3) Literature review
- (4) Specific study objectives
- (5) Research methods
- (6) Subjects
 - a. Inclusion / exclusion criteria
 - b. Sampling
 - c. Recruitment plans
 - d. Method of assignment to study group
- (7) Data collection
 - a. Variables: outcomes, predictors, confounders
 - b. Measures/ instruments
 - c. Procedures

NOTE: Consideration should be given to use of data already available from clinical procedures conducted as part of routine care when possible
- (8) Intervention
- (9) Statistical considerations
 - a. Sample size
 - b. Data analysis

2. Activities Requiring R&D Committee Review

- A. All research that meets the definition of “VA Research” must be reviewed and approved by the STVHCS R&D Committee and its subcommittee(s) prior to initiation of the research.
- B. Research that is being submitted by the STVHCS to VA, other Federal agencies, or other entities for funding consideration must undergo a preliminary review and receive concurrence from the R&D Committee prior to submission of the protocol.
- C. The following activities are not considered research and therefore are not under the purview of the VA R&D Committee:
 - (1) Quality Improvement projects that are not designed or intended produce generalizable results
 - (2) Meta-analysis of published studies
 - (3) Case Reports that are not designed or intended produce generalizable results
 - (4) Literature Searches that are not designed or intended produce generalizable results

- D. If you are unsure whether an activity or proposed project requires R&D approval, contact the STVHCS Research Office (contact information provided in Section 1)

3. Protocol Submission Process

Research protocol submissions for proposed VA human research studies are submitted to the STVHCS R&D office. Investigators are encouraged to discuss new protocols with the R&D Office before submitting the application. All application forms are available from the STVHCS Research Service Website at <http://www.south-texas.med.va.gov/research/>

A complete protocol submission should include the following:

- (1) R&D Checklist
- (2) Request to Review Research Proposal
Must be signed by the Principal Investigator and Service Chief
Printed on Green Paper
- (3) A copy of the complete research protocol
- (4) A one-page abstract
- (5) Conflict of Interest Disclosure form
Signed by all key research personnel
- (6) VA Form 10-1086 – VA Research Consent form
- (7) Form 10-9012 – Investigational Drug Information Record for each drug, compound, or test substance to be used in the study
- (8) Statement of Clinical Research Impact on the appropriate VA Hospital services
- (9) Industry-supported project costs associated with human subjects
- (10) Disclaimer from commercial sponsor if industry-sponsored
- (11) Commercial sponsor funding memo, if funds are not to be administered by the Biomedical Research Foundation of South Texas
- (12) VA Form 10-5368, Investigator Data Sheet, if this is first research proposal submitted to the STVHCS
- (13) Curriculum vitae – one copy for each investigator if not previously provided
- (14) Research Data security worksheet

4. Subcommittees of the R&D Committee

The STVHCS R&D Committee has established Subcommittees to ensure the safety and protection of human and animal subjects, the safety of personnel engaged in research, and for the efficient and effective oversight of research resources. The R&D Committee cannot approve a protocol without the approval of the appropriate subcommittee, so submission of the protocol to the appropriate subcommittee should occur before or concurrently with the R&D Committee submission.

The R&D Committee and its subcommittees do not answer to individuals, departments, or units that rely on them for the review of their research. The PI of each submitted protocol must ensure

there is no undue influence asserted by any member of the research team toward any review or oversight committee or committee member. Each of the Subcommittees function independently in its review and oversight of research, and one Subcommittee cannot exert undue influence on the independent review and conclusions of another. Any study personnel who becomes aware of attempts to inappropriately influence a review committee should report the incident to the IRB Director, ACOS for R&D, Research Compliance Office, or Medical Center Director. Allegations of attempts to exert undue influence will be referred to the Research Compliance Officer for investigation, and findings and recommendations for action resulting from the investigation will be reported to the Medical Center Director, and IRB or R&D Committee as appropriate, for corrective action.

A. Subcommittee on Human Studies (Institutional Review Board; IRB)

The UTHSCSA IRB is the IRB of record for the STVHCS. Protocols may be submitted first to the IRB, or in parallel to the IRB and R&D Committee. The R&D Committee will not review a protocol if it has not been approved by, or submitted to, the IRB. Instructions and forms for IRB submission can be found on the IRB website. Please refer to the ***IRB Protocol Submission Checklist*** to ensure that you have completed all required documents for submission. The IRB application does not need to be submitted to the STVHCS R&D Office.

No human research project is granted final approval by the R&D Committee until it has been approved by the IRB.

B. Subcommittee on Research Safety (SRS)

The SRS is charged with protection of all research personnel to ensure safe research practices and physical and biosecurity of the research facility. No research project involving potential biohazards, chemical hazards, physical hazards or radiation hazards will be granted final approval by the R&D Committee until it has been approved by the SRS.

C. Radiation Safety Committee

Human subject research involving ionizing radiation or radioactive substances, multiple X-Rays, CT Scan or other radiological procedures, must be reviewed and approved by the STVHCS Radiation Safety Committee. Specific documentation must be submitted to the R&D Committee for review of any research radiation issues. No research project involving radiation will be granted final approval by the R&D Committee until it has been approved by the Radiation Committee.

5. Exempt Research

The Department of Health and Human Services (DHHS) and FDA regulations apply to research involving human subjects, but there are some categories of research are considered exempt from these regulations. To qualify as an exempt study, the research must fall within one of the

specific regulatory categories. The investigator does not have the authority to determine if a study meets criteria for exempt status. The UTHSCSA IRB Director or his/her designated reviewers determines if the study qualifies for an exempt status. Any study that the IRB Director or his/her designated reviewers believes is not exempt must receive either expedited or convened review by the IRB.

Unless otherwise required by Department or Agency heads [Please note: this reference is to government department or agency heads, not to local STVHCS or UTSCSA department directors], research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from Federal regulations:

A. Educational Research 45CFR46.101(b)(1)

The research will be conducted in an established or commonly accepted educational setting, involving normal educational practices, such as:

- (1) Research on regular and special education instructional strategies
- (2) Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (3) AND All of the following must be true:
 - i. The research is minimal risk.
 - ii. The research does not involve prisoners as participants.
 - iii. The research is not FDA regulated. See UTHSCSA IRB definition of FDA regulated at <http://research.uthscsa.edu/irb/GLOSSARY%20OF%20IRB%20TERMS.doc>

B. Research using surveys, interviews, educational testing 45CFR46.101(b)(2)

The research involves the use of:

- (1) Educational tests (cognitive, diagnostic, aptitude, achievement)
- (2) Surveys, interviews or observations of public behavior including:
 - i. Observations of public behavior not involving children
 - ii. Observations of public behavior involving children where the investigator does not participate in the activities being observed
 - iii. Interview procedures not involving children
 - iv. Survey procedures not involving children
- (3) The research is minimal risk.
- (4) The research must meet at least one of these additional requirements:
 - i. The nature of the information obtained in this study does not reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, reputation, or loss of insurability
 - ii. The nature of the information obtained does represent a risk to subjects. However, the information obtained will not be recorded so that the subjects can be identified directly or indirectly (through identifiers linked to the subjects e.g., codes)

C. Research using surveys, interviews, educational testing involving elected/appointed public officials or where confidentiality of data is protected by federal statute **45CFR46.101(b)(3)**

The research involves the use of:

- (1) Educational tests (cognitive, diagnostic, aptitude, achievement)
- (2) Observations of public behavior not involving children
- (3) Observations of public behavior involving children where the investigator does not participate in the activities being observed
- (4) Interview procedures not involving children
- (5) Survey procedures not involving children
- (6) The research is minimal risk.
- (7) The research must meet at least one of these additional requirements
 - i. The human subjects are elected or appointed public officials or candidates for public office
 - ii. Federal statute requires without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter

D. Research using existing specimens/data **45CFR46.101(b)(4)**

This research involves the collection or study of:

- (1) Existing data
- (2) Existing documents
- (3) Existing records
- (4) Existing pathological specimens
- (5) Existing diagnostic specimens

Note: Existing = data/specimens that exist now, are on the shelf. Existing does not mean data or specimens that are normally collected but have yet to be recorded / collected
- (6) If the information to be collected is from a source which contains identifiable information (i.e. medical records or documents, specimens, etc.) You must also complete a HIPAA Waiver of Authorization request to the IRB
- (7) The research is minimal risk
- (8) The research must meet at least one of these additional requirements
 - i. The information obtained will not be recorded so that the subjects can be identified directly or indirectly (through identifiers linked to the subjects e.g., codes)
 - ii. These sources are publicly available (This choice is rarely applicable to medical research studies)
- (9) The research does not involve prisoners as participants

- (10) The research is not FDA regulated. See UTHSCSA IRB definition of FDA regulated at <http://research.uthscsa.edu/irb/GLOSSARY%20OF%20IRB%20TERMS.doc>

E. Research or Demonstration Projects Approved by Federal Department/Agency Head 45CFR46.101(b)(5)

NOTE for VA studies: The determination of exempt status for these research and demonstration projects must be made by the Under Secretary for Health on behalf of the Secretary of Veterans Affairs, after consultation with Office of Research and Development, the Office of Research Oversight, the Office of General Counsel, and other experts, as appropriate.

- (1) The project is a research and demonstration project.
- (2) The research is minimal risk.
- (3) The research is conducted by or subject to the approval of federal Department or Agency heads
- (4) The research is designed to study, evaluate, or otherwise examine
 - i. Public benefit or service programs
 - ii. Procedures for obtaining benefits or services under public benefit or service programs
 - iii. Possible changes in or alternatives to public benefit or service programs
 - iv. Possible changes in methods or levels of payment for benefits or services under public benefit or service programs
- (3) The program under study delivers a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- (4) The research is conducted pursuant to specific federal statutory requirement.
- (5) There is no statutory requirement that an IRB review the research.
- (6) The research does not involve significant physical invasions or intrusions upon the privacy of participants.
- (7) The research does not involve prisoners as participants.
- (8) The research is not FDA regulated. See UTHSCSA IRB definition of FDA regulated at <http://research.uthscsa.edu/irb/GLOSSARY%20OF%20IRB%20TERMS.doc>

F. Taste and food quality evaluation or consumer acceptance 45CFR46.101(b)(6)

This study involves taste and food quality evaluation or consumer acceptance studies.

- (1) The research is minimal risk
- (2) The research must met at least one of these additional requirements
 - i. Wholesome foods without additives are consumed
 - ii. If a food is consumed that contains a food ingredient or an agricultural chemical or environmental contaminant, the food ingredient or

agricultural chemical or environmental contaminant is at or below the level and for a use found to be safe by one of the following:

- a. The Food and Drug Administration
- b. The Environmental Protection Agency
- c. The Food Safety and Inspection Service of the U.S. Department of Agriculture

For additional information regarding exempt research refer to the Health and Human Services Website at <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm> , the UTHSCSA Website at <http://research.uthscsa.edu/irb/> (Form B-4), or contact the UTHSCSA IRB Director at (210) 567-2357.

VA regulations require an annual review of all research including those protocols that have been determined to be exempt. If your research protocol has been determined to be exempt, the STVHCS R&D requires that you submit an annual report of research activities for your protocol. This report will be sent from the R&D office directly to the investigator for completion prior to review and reapproval.

6. Protocol Amendments

Any amendment that creates changes to the research protocol, recruitment procedures, VA consent form(s) or HIPAA Authorization document(s), must have IRB approval prior to implementation. A copy of the IRB approval letter along with any consent documents, HIPAA Authorizations, and/or recruitment materials for use at the VA must be sent the R&D office.

7. Continuing Review

The STVHCS R&D Committee and UTHSCSA IRB must review and approve all approved research protocols at least annually. Applications for continuing review should be submitted to the IRB in a timely manner so that they may be reviewed and approved prior to the expiration of IRB approval. The IRB continuing review documents will be forwarded to the R&D Committee for continuing review.

In addition to the UTHSCSA IRB continuing review, the R&D office will forward a STVHCS Continuing Review Form to each investigator. This form will collect the following additional information:

- (1) Changes in project personnel
- (2) Changes in the duties or procedures for study personnel that would require an updated Scope of Practice.
- (3) Changes in the financial or non-financial arrangements for investigators or study personnel that would require an updated conflict of interest disclosure
- (4) Changes in the collection, storage, or use of VA-sensitive research data for the project that would require an updated VA research data security checklist
- (5) Changes to the VA Form 10-9012 (Investigational Drug Record Form)

- (6) Project update/summary for EXEMPT research protocols and for the final report of non-exempt research protocols
- (7) Changes to the Research Protocol Safety Survey if applicable

Approval for a research protocol may expire because of failure to meet reporting (e.g. Continuing Review or CITI Training requirements) deadlines. In this case, the PI will be notified that activities related to the research protocol must immediately cease, with the exception of those activities required to ensure the safety of subjects already enrolled in the protocol. The expiration in approval of the protocol will be corrected upon receipt and satisfactory review and approval of the required documentation.

8. HIPAA Authorizations for Research

The IRB routinely evaluates the VA HIPAA Authorizations or request for a waiver as part of their review of the protocol application and recruitment materials. However, the IRB does not serve as the privacy board for the STVHCS. Final review and approval of HIPAA Authorizations or waivers are conducted by the Privacy Office at the STVHCS prior to R&D approval.

SECTION 10: Monitoring Subjects for Potential Harm and Reporting Requirements

1. Development of a Data Safety Monitoring Plan (DSMP)

A DSMP is a written plan designed to ensure the safety of clinical research participants and the validity and integrity of research data. It is a local contract between the PI and the IRB verifying the ethical responsibility of the PI and their study staff to research participants. When implemented a DSMP provides a process to determine if any of the treatment procedures practiced for a specific protocol should be altered or stopped to protect participants.

The following studies require a DSMP:

- (1) All studies considered to be more than minimal risk
- (2) Studies involving high risk populations and/or high risk therapies
- (3) Multi-site research where UTHSCSA is the coordinating site
- (4) Studies where there is an NIH or FDA requirement for a plan
- (5) Studies when requested by the IRB

Studies which do not require a DSMP include:

- (1) Studies which qualify for exempt review
- (2) Studies that do not involve contact with a living human subject
- (3) Minimal risk studies on a case by case basis as determined by the IRB

The local PI responsibilities for the DSMP include:

- (1) Capturing and collecting data
- (2) Monitoring collected data
- (3) Interpretation and analysis of collected data
- (4) Reporting results of analysis
- (5) Implementing actions based on analysis if needed

The DSMP should be commensurate with the level of risk and with the size and complexity of the study. Types of data and events being captured should include:

- (1) Adverse events
- (2) Serious adverse events
- (3) Deaths
- (4) Disease or treatment specific events - Anticipated or Unanticipated
- (5) Expected frequency of events (e.g. reasonably expected)

As part of the DSMP individual subjects should be assessed for:

- (1) Nature, severity, and frequency of events
- (2) An event occurring more frequently than anticipated, which may need to be considered a UPIRSO

(3) Major safety concerns of the study

The PI compiles a brief evaluation summary from the data collected as part of the DSMP.

- (1) If the evaluation constitutes an unanticipated problem involving risk to subjects or others (UPIRSO):
 - a. The PI must forward the evaluation summary to the IRB immediately
 - b. The UPIRSO form must be attached explaining how the evaluation constitutes a UPIRSO
- (2) If the evaluation does NOT constitute an UPIRSO, the PI must forward to the IRB a summary of all evaluations as part of continuing review at least annually

The DSMP should have a plan of action which may include, but is not limited to:

- (1) Amendment to the protocol
- (2) Protocol suspensions
- (3) Changes to enrollment procedures
- (4) Changes to data collection plan or study forms
- (5) Notification of past and present subjects

For additional information regarding DSMP refer to the UTHSCSA IRB website <http://research.uthscsa.edu/irb/> Form R: Human Use Research Monitoring Participant Safety and Data Integrity.

2. Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs)

The purpose of reporting unanticipated problems involving risk to subjects or others is to protect the rights and welfare of participants in human subject research. Investigators involved in human subject research at the STVHCS are required to promptly report possible unanticipated problems involving risk to subjects or others (UPIRSO) as defined by the IRB ([http://research.uthscsa.edu/irb/GLOSSARY OF OIRB TERMS.doc](http://research.uthscsa.edu/irb/GLOSSARY%20OF%20OIRB%20TERMS.doc)), and according to the IRB UPIRSO policy ([http://research.uthscsa.edu/irb/policy/UPIRSO Policy and Procedure.doc](http://research.uthscsa.edu/irb/policy/UPIRSO%20Policy%20and%20Procedure.doc)) . UPIRSOs that involve the loss or compromise of individually identifiable information of a research subject should also be reported promptly to the Privacy Officer. UPIRSOs that involve the violation of information security requirements should also be reported promptly to the Information Security Officer.

SECTION 11: Conflict of Interest / Statement of Disclosure

The VA has an obligation to preserve public trust in the integrity and quality of research carried out by its investigators. Appropriate mechanisms must be in place to ensure that actual or perceived financial conflicts of interest do not undermine that trust. A financial conflict or perceived conflict of interest occurs when any financial arrangement, situation or action affects or is perceived to exert inappropriate influence on the design, review, conduct, results or reporting of research activities or findings. The impact of the conflict may occur in any phase of the research.

All VA researchers must sign and submit to the R&D Office a conflict of interest disclosure statement prior to conducting research within the VA system. A conflict of interest disclosure is required for each principal investigator, co-principal investigator, investigator, and each collaborator (all research personnel approved for a protocol). The principal investigator must ensure that all investigators or other individuals associated with the protocol have submitted their disclosure forms.

Distribution of the conflict of interest disclosure is limited to only those persons who are required to review it as part of their responsibilities in order to maintain the investigators privacy and confidentiality.

A conflict of interest disclosure may be initiated at any time including when first appointed as a VA investigator but must occur prior to the submission of a protocol to any research review committee such as the IRB or R&D committee.

The investigator must update the disclosure when there are any changes (e.g. new conflicts of interest are identified or current ones cease to exist). When submitting a protocol for continuing review in which there has been no change in the disclosure form, the investigator submits a statement certifying that the financial conflicts disclosed during initial review have not changed. If an updated disclosure form has been submitted, this information must be available with the continuing review materials for R&D review prior to continued approval being granted.

A significant financial conflict of interest includes, but is not limited to the following monetary interests:

- (1) Non-VA salary or other payments for services from private or for-profit entities (e.g., consulting fees or honoraria)
- (2) Compensation to the investigator if the amount of the compensation could be affected by study outcome
- (3) Equity interests (e.g., stocks, stock options, or other ownership interests)
- (4) Intellectual property rights (e.g., patents, copyrights, and royalties from such rights) that would reasonably be expected or appear to affect the proposed research
- (5) Consulting fees, honoraria, gifts, or other “in kind” compensation from a financially interested company for any purpose not directly related to the reasonable costs of the research that in the aggregate have in the prior calendar year exceeded \$10,000, or are expected to exceed that amount in the next 12 months.

- (6) Any on-royalty payments or entitlements to payments in connection with the proposed research that are not directly related to the reasonable costs of the research. This includes any bonuses or milestone payments to the investigators in excess of reasonable costs incurred.
- (7) Service as an officer, director, or in any other fiduciary role for a company with financial interests in the proposed research.

Significant financial conflict of interest does NOT include:

- (1) Salary, royalties, or other remuneration from the applicant's home institution
- (2) Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities
- (3) Income from service on advisory committees or review panels for public or non-profit entities

If an investigator fails to comply with the financial conflicts of interest policy or with corrective actions determined by the reviewing committees, the following may be initiated:

- (1) Termination of the research protocol
- (2) Removal of the investigator from the research protocol team
- (3) Revocation of the privilege to conduct research

The investigator may also be sanctioned by the Public Health Service, the FDA, or other applicable entities depending on the seriousness of the non-compliance and the determination of the research sponsor. Violation of the Standards of Ethical Conduct for Employees of the Executive Branch may result in corrective or disciplinary actions. Violation of criminal conflict of interest statutes may result in referral to the U.S. Department of Justice. Punishment may include civil and criminal penalties.

SECTION 12: Security of Research Data

Data Security and Privacy is the protection of confidential information, including technical procedures for maintaining the security and integrity of research data.

1. VA Sensitive Research Data

A. Definition of VA-sensitive research data:

- (1) Individually-identifiable research data that is collected on a veteran subject through a STVHCS-approved protocol
- (2) Individually-identifiable research data that is collected on a veteran or non-veteran within the STVHCS
- (3) Individually-identifiable research data collected as part of a VA-funded study

B. Not VA-sensitive research data:

- (1) Non-identifiable data (includes none of the 18 HIPAA identifiers and the remaining information cannot be used to determine the identity of an individual directly or through any statistical analysis)
- (2) Collected on non-veterans outside of the VA on a non-VA funded project

2. Storage of VA-sensitive Research Data

A. Electronic Data

- (1) Because of the risk of loss or compromise of electronically stored data, and the potential consequences to the VA mission, all VA-sensitive electronic data must be stored within the VA system (behind the VA firewall).
- (2) Because the information Security standards for the UTHSCSA are different from the VA, VA-sensitive electronic data cannot be stored on UTHSCSA computers, servers, or within the UTHSCSA system.
- (3) It is recommended that VA-sensitive research data be stored on the VA research server, which can be accessed directly through the VA network from a VA computer, or through VPN from a non-VA computer (from anywhere at anytime).
- (4) For instructions on how to set up a folder on the VA server and to get VPN access please contact the Research Office (Angela Casas x15523) or the Information Security Officer (Gerald Steward x14734).
- (5) In rare instances where VA-sensitive data must be stored on an individual VA computer workstation, that computer must be encrypted.

B. Paper Data

- (1) Research data that is stored on a paper copy (e.g. case report forms, data forms, etc) carries a lower risk of loss or compromise than electronic data.

- (2) Physical security controls are required for the storage of VA-sensitive data stored on paper.
- (3) The data must be stored in a locked cabinet in a locked room, in which access is restricted to study staff (only study staff has a key to the room and cabinets).
- (4) Because the physical security controls in place at the UTHSCSA are consistent with the VA standard, it is acceptable for VA-sensitive research data to be stored at the UTHSCSA, provided the physical security arrangements are inspected and approved by VA staff.

C. Research Specimens

- (1) Research specimens must be secured in a locked room and/or a locked freezer, refrigerator, or cabinet with access restricted to the research staff.
- (2) Research specimens may be stored at the UTHSCSA provided they meet these criteria and the storage space and conditions are inspected and approved by VA staff.

D. Keys to Coding Systems

- (1) If non-identifiable information (data or specimens) is linked to identifiable information with the use of data or specimen logs, these logs are VA-sensitive research data.
- (2) If the log is maintained on paper it must be stored in a locked cabinet in a locked room.
- (3) If there is an electronic log with identifiable information it must be stored on the VA research server.
- (4) A key to a coding system should be stored in a location separate from the data or specimens to which it is linked.

E. Access to the identifiable data must be limited to authorized individuals who are designated on the VA approved protocol.

3. Certification

All VA research protocols must be certified by the ACOS/Research, Information Security Officer, Privacy Officer and Medical Center Director as meeting the standards for research data security before the research protocol can be activated.

4. Loss or Compromise of VA-sensitive Research Data

Any loss or compromise of the VA-sensitive research data must be reported promptly to the ACOS for Research and Information Security Officer at the STVHCS.

5. Change in Location of Research Data

Any transmission, transport, or use of the VA-sensitive data outside the approved location must be approved by the ACOS for Research, Information Security Officer, and Privacy Officer of the STVHCS.

6. Inspection of Research Data Storage

Off-site space used to store any VA-sensitive research data must be inspected and approved as meeting the VA standards for physical security by the ACOS for Research, and Information Security Officer of the STVHCS. Documentation of this approval will be maintained with the research protocol in the STVHCS Research Office.

SECTION 13: Research Record Keeping

1. Maintaining Subject Privacy and Confidentiality of Their Research Data

Investigators should maintain the privacy of the research subject and handle records in a way that assures the confidentiality of individually identifiable subject data, except when required by law or released with the permission of the subject. Subjects have the right to be protected against invasion of their privacy, to expect that their personal dignity will be maintained, and that the confidentiality of private information will be preserved. The more sensitive the research material, the greater care required in obtaining, handling, and storing data.

To protect subject confidentiality, the following guidelines are applicable:

- (1) Limit recording of personal information to that which is essential to the research.
- (2) Store personally identifiable data securely and limit access to the PI and authorized staff; subject records should be stored in a locked file cabinet or office.
- (3) Code data as early as possible in the research process, and plan for the ultimate disposition of the code linking the data to individual subjects.

2. Procedures for Long Term Storage of Records

- A. The Principal Investigator will identify on the Data Security Checklist where research records will be stored and for how long after completion of the study.
- B. If assistance in long-term storage is required, the Principal Investigator or study staff should contact the R&D office at (210)-617-5123 for a key and access to the R&D storage area.
- C. The Principal Investigator and study staff will be responsible for labeling of the storage boxes and transport to the R&D storage area.
- D. The following information must be located on the outside of each box:
 - (1) Responsible Investigator
 - (2) Investigator Contact number
 - (3) Protocol name
 - (4) Sponsor
 - (5) Sponsor contact number
 - (6) Dates research was conducted
 - (7) Destruction date for records
 - (8) Box # out of total number of boxes (i.e. box 1 of 2)
 - (9) Electronic Media type and quantity, if applicable
 - (10) Description of Contents (i.e. CRFs, Binders, Tapes)
- E. The Responsible Investigator must notify the R&D office of any changes in the above listed items. If the Responsible Investigator leaves the STVHCS, they must notify

- the R&D office of the name of the new Responsible Investigator. This is a requirement for out processing from the facility.
- F. Study records must be retained for a minimum of 5 years after the completion of the study as per VHA policy. Records may be stored longer if required by the study sponsor.
 - G. All records must be accessible for inspection and copying by authorized representatives of VA, OHRP, FDA and other authorized entities at reasonable times and in a reasonable manner.
 - H. The R&D office will maintain a log of all stored research records in the R&D storage area. The log will contain the following information:
 - (1) Responsible Investigator
 - (2) Investigator contact number
 - (3) Protocol name
 - (4) Sponsor
 - (5) Sponsor contact number
 - (6) Dates research was conducted
 - (7) Number of boxes
 - (8) Destruction date
 - I. The Responsible Investigator and/or study staff will be contacted for destruction of the stored records based on the destruction date provided.

3. Destruction of Clinical Research Records

When research related paper documents are no longer needed they should be destroyed by cross-cut shredding. When research related electronic data is no longer needed it should be destroyed by a method rendering it unreadable, undecipherable, and irretrievable. VA regulations require sanitization of VA sensitive data from electronic equipment before the equipment is disposed of. This sanitization process must cause the removal of all VA sensitive data from information systems storage devices and render the data from these systems unreadable. The VA OI&T Department should be contacted to perform media sanitization which is in compliance with VA media sanitization policy and procedures.

SECTION 14: Tissue Banking

If a human subject research study involves the collection and/or storage of tissue, the tissue may only be stored in a VA approved tissue bank. A research protocol application that involves the use of tissue stored in a non-VA approved tissue bank must be submitted to Office of Research and Development (ORD) by the Associate Chief of Staff for Research at the STVHCS on behalf of the Principal Investigator/Project Director for approval. Applications cannot be submitted by non-VA investigators. Please contact the R&D Office for additional information on the procedures for preparing a tissue bank approval application.

SECTION 15: Human Subjects Concerns/Complaints/Allegations of Research Improperities

Investigators and study staff must be sensitive toward the needs of their research participants and must respond to all complaints, concerns, suggestions, or requests for additional information in a positive and timely manner. In addition, all investigators and study staff are responsible for bringing allegations of research improprieties to the attention of the IRB or R&D Office to assure appropriate actions are initiated. Research non-compliance or alleged improprieties may be identified through self-reporting by the principal investigator or by other members of the study team.

A research subject or anyone with a concern/complaint regarding a research study involving human subjects may raise the concern/complaint with the PI or study staff. Upon receipt of a concern/complaint or allegation, the PI or study staff should gather the following information from the complainant:

- (1) Subject's (or complainant's) name, address, and phone number (This information is NOT MANDATORY, and a caller may report an incident anonymously; however, advise the caller that a thorough review may not be possible, and that, without this information, follow-up responses to the subject are not feasible.);
- (2) Study protocol title (or acronym)
- (3) Date(s) of the incident;
- (4) A summary of the complaint or concern.

The PI or study staff should promptly evaluate the concern/complaint on a case-by-case basis and makes every effort to correct the issue(s) at the administrative level.

The PI or study staff may forward the concern/complaint or allegation of research impropriety to the ACOS for R&D or the Assistant Chief for Clinical Research and the complainant will be contacted by the ACOS for R&D or the Assistant Director for Clinical Research to gather all required information.

All concerns/complaints should be handled in a confidential manner to the extent allowed by law. Access to information concerning the complaint should be limited to employees with responsibilities that require knowledge of the concern/complaint.

If the alleged impropriety involves potential harm to subjects or others, the R&D Chairman and the IRB Director must be notified for immediate action pending formal inquiry. Notification to the R&D Chairman and the IRB Director can be through ACOS for R&D or the Assistant Chief for Clinical Research. If appropriate, the ACOS for R&D or the Assistant Chief for Clinical Research will also provide a report to the Compliance Office, General Counsel, STVHCS Chief of Staff, and STVHCS Director for solicitation of additional input.

The IRB and R&D Chairs or his/her designees, in collaboration with the ACOS for R&D and the Assistant Chief for Clinical Research, ensure appropriate response to each complaint and reports the action(s) taken to the IRB and R&D Committees. If the complaint or concern is of a minor nature (i.e. misunderstanding, clerical or administrative issue such as a payment) the issue may be resolved without bringing it forth for an IRB or R&D committee vote. Major issues such

as failure to acquire signed informed consent from potential subjects (if required), are presented to the IRB and R&D Committee and any actions are voted on. All actions taken are at the institutional level and appropriate for the circumstances, and the final course of action is entirely dependent on the nature, severity, and degree of seriousness of the findings.

If an allegation of research misconduct is identified, it is handled in accordance with VHA Handbook 1058.2. Refer to the STVHCS Misconduct Policy and SOP for additional information.

Problems that cannot be resolved by the PI or within the R&D Service will be referred to the Chief of Staff Office.

SECTION 16: External Clinical Research Monitoring Visits

Investigator records (i.e., regulatory documents, case report forms, correspondence, study files) and subject's medical records [i.e., source documents, Computerized Patient Records System (CPRS), informed consent documents] are subject to inspection and monitoring by external agencies [i.e., pharmaceutical companies, study sponsors, Contract Research Organizations (CROs), VA Cooperative Studies Program (CSP) Monitor]. These site visits may be routine or conducted for specific causes. In accordance with the facilities Human Subjects Protection Program (HRPP), any findings or issues of concern resulting from a monitoring visit must be forwarded to the STVHCS R&D Office to assess if they are appropriately addressed and to assure the appropriate facility officials and committees are notified.

1. Upon Notice of a Monitoring Visit

- A. The Assistant Chief for Clinical Research is to be notified of all monitoring visits by external monitoring agencies as soon as possible. This is the responsibility of the research staff person who schedules or confirms the monitoring visit.

- (1) Notification should be by email to KimberlyK.Summers@va.gov.
- (2) If the monitoring visit is unscheduled, the Assistant Chief for Clinical Research is to be notified as soon as the study personnel are aware of the visit. This may be done by telephone at 210-617-5123.

2. At the Time of the Monitoring Visit

- A. The CRO or study monitor must sign in as a visitor at the R&D Office and receive a visitor's badge. A Research Monitor Log will be maintained by the R&D Office which includes the following information:

Date	Study	PI/Coordinator	Purpose	Monitor Name	Check-in time
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- B. The PI or designated study staff must inform the monitor that any potential or actual serious findings must be conveyed to the investigator and the Assistant Chief for Clinical Research during an exit interview. Findings that require an exit interview include but are not limited to:

- (1) Any suspicions or concerns that serious non-compliance may exist
- (2) All findings of serious non-compliance with study protocol, Institutional Review Board (IRB) requirements or applicable regulations and policies (i.e., failure to consent subjects, entering subjects who do not meet entrance criteria into protocols, failure to report serious or unexpected adverse events)
- (3) Monitoring visits conducted by a regulatory agency (FDA, OHRP)

- C. The CRO or study monitor must present a signed External Monitor Agreement form (available at the R&D Office at the time of check-in or on the STVHCS R&D Research website) to the R&D office prior to initiation of the site visit.
 - (1) During the monitoring activities, the external monitor may only access information and research data that is necessary and in accordance with the approved protocol.
 - (2) The external monitor may not review data in the electronic medical record except under the direct supervision of the STVHCS research staff.
- D. The CRO or study monitor must complete and sign the “STVHCS Report of Clinical Research Monitoring Visit” form (available at the R&D Office at the time of check-in or on the STVHCS R&D Research website) prior to departure from the facility. Completion of this form is required independent of the findings associated with the visit.

3. Following the Monitoring Visit

- A. The PI or designated study staff must forward all “STVHCS Report of Clinical Research Monitoring Visit” forms to the R&D Office
- B. All monitoring reports with potential or actual serious findings will be evaluated in accordance with the STVHCS UPIRSO and Noncompliance Policies to implement the appropriate reporting mechanisms. These reports will also be forwarded to the QA Subcommittee for review and recommendations.

SECTION 17: Investigator and Study Staff Training Opportunities

1. On-site Assessment and Training for Investigators and Research Staff

The R&D Office staff, the ACOS for R&D, and the Assistant Chief for Clinical Research are available to conduct on-site assessment and training when requested by a STVHCS Investigator, their study personnel, or the R&D Committee.

2. Electronic Communication Network for Research Study Team Members

The R&D office maintains a Research Study Members email group of all active human subjects' investigators, study coordinators, and other key study personnel. This establishes an ongoing method for regular feedback and dialogue between the R&D Office, principal investigators, and key research coordinators involved in the day-to-day implementation and operational functions of human research projects.

3. Monthly Education and Training Sessions for Research Study Team Members

The ACOS for R&D and the Assistant Chief for Clinical Research routinely conduct needs assessments and review of newly drafted documents and/or procedures for investigator and study staff training opportunities. Monthly interactive training sessions are conducted to disseminate new information. Handouts for each training session are provided to all Research Study Team Members and are posted on the Research Service website for future reference.

4. UTHSCSA Clinical Research Training Course

The STVHCS participates with the UTHSCSA in providing an 8-hour training course on "Conducting Clinical Research". All personnel involved in human subjects' research at the STVHCS are strongly encouraged to participate in this course, which is offered 3 times per year. For additional information and scheduled training dates refer to the UTHSCSA Office of Clinical Research (OCR) website at <http://research.uthscsa.edu/ocr/index.shtml>

5. UTHSCSA IRB Training Sessions

IRB forums which review policies and procedures for UTHSCSA IRB submissions are held on a regular basis. For additional information and scheduled training dates and times refer to the UTHSCSA IRB website at <http://research.uthscsa.edu/irb/index.shtml>

SECTION 18: Policy and Procedures of Oversight of VA Studies

The VA Research Compliance Office will randomly audit research protocols that have enrolled VA subjects. The Research Compliance Office will notify the PI when an audit will be performed, and will request in writing the information necessary to perform the audit. It is the Principal Investigator's responsibility to provide all requested information and documents to the compliance auditor for review and oversight of the research. Results of all audits and any necessary corrective actions will be communicated to the PI in writing. The findings of the audit will also be reported to the R & D Committee via the QA Subcommittee.

APPENDIX A: DETERMINING WHETHER AN ACTIVITY IS HUMAN RESEARCH

In accordance with federal and institutional regulations and prior to project implementation, the IRB must approve any undertaking in which STVHCS staff conducts non-exempt human research. This Appendix supplements the STVHCS Human Research Protection Program Policy (PM 151-08-03) by providing additional information related to determining whether an activity is research involving human participants and covered by the Federal Regulations. In general, any activity that meets either the Department of Health and Human Services (DHHS) definition of both “research” and “human subjects” or the Food and Drug Administration (FDA) definitions of both “clinical investigation” and “human subjects” is considered human research and requires review and approval by the IRB.

It is the responsibility of each investigator to seek IRB approval prior to initiation of any non-exempt research involving human subjects or before conducting any clinical investigation. The investigator is responsible for making a preliminary decision regarding whether his/her activities meet either (a) the Department of Health and Human Services (DHHS) definitions of both “research” and “human subjects” or (b) the FDA definitions of both “clinical investigations” and “human subjects”. A worksheet titled “Determining Whether An Activity is Research Involving Human Participants” is also available on the UTHSCSA IRB website (<http://research.uthscsa.edu/irb/sop.shtml>) to guide the investigator in making this decision. The investigator may also contact the STVHCS R&D Office, the UTHSCSA OIRB staff, the IRB Chair, or IRB members for advice on the application of the federal regulations and local policy.

The following sequential assessment is used when evaluating a particular activity to determine whether the activity is human research:

1. Step 1: Is the activity “Human Research” according to DHHS regulations?

a. Criterion 1. The activity is research if either of the following is true:

1. It is part of a systematic investigation (including research development, testing and evaluation) to test a hypothesis and permit conclusions to be drawn, usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective; **or**,

2. *It is designed to (e.g., the primary purpose) contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships, or published in medical journals as research)*

If either (1) or (2) are true, proceed to criterion 2.

If neither (1) nor (2) are true, the activity is not “Human Research” according to DHHS regulations. Go to Step 2 to determine whether the activity is “Human Research” according to FDA regulations.

b. **Criterion 2.** The research involves human participants because:

1. *The investigator will obtain data about living individuals; **and***
2. *The investigator will obtain this data through intervention or interaction with those participants; **or***
3. *The information obtained by the investigator is **both** private (i.e., the information is private because it includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public) **AND** identifiable (i.e., the information is individually identifiable because the identity of the participant may be readily ascertained by the investigator or associated with the information.).*

If the statements in criterion 2 are true, the activity is human research according to DHHS regulations. Go to Step 2 to determine whether the study is human research according to the FDA regulations.

If the statements in criterion 2 are not true, the activity is not human research according to DHHS regulations. Go to Step 2 to determine whether the study is human research according to the FDA regulations.

2. **Step 2:** Is the activity “Human Research” according to FDA regulations?

a. **Criterion 1.** *The activity involves an FDA regulated test article because at least one of the statements below is true:*

1. *The activity involves the use of a drug, other than the use of a marketed drug in the course of medical practice; **or***
2. *The activity involves the use of a device to evaluate safety or effectiveness of that device; **or***
3. *Data from the activity will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product.*

If any of the above is true, proceed to criterion 2.

If none of the above is true, then the activity is not Human Research according to FDA regulations.

b. **Criterion 2.** The activity involving an FDA-regulated test article involves human participants because at least one of the statements below is true:

1. *The test article will be used on one or more humans; **or***

*2. The data obtained from controls will be submitted to, or held for inspection by the FDA in support of a marketing or research application for an FDA-regulated product; **or***

3. The data obtained from use of a device on tissue specimens will be submitted to, or held for inspection by, the FDA in support of a marketing application or research application for an FDA regulated product.

If any of the above is true, the activity is human research according to FDA regulations.

If none of the above is true, then the activity is not Human Research according to FDA regulations.

3. Step 3: Summary of “Human Research” determinations (DHHS & FDA)

a. DHHS - If the activity is considered research (Step 1, criterion 1) and involves human participants (Step 1, criterion 2), it is considered human research according to the DHHS and requires IRB approval.

b. FDA – If the activity involves an FDA regulated test article (Step 2, criterion 1) and involves human participants (Step 2, criterion 2), it is considered human research according to the FDA and requires IRB approval.

4. The following are examples of human subject research studies that must be reviewed and approved by the IRB.

Masters thesis/Doctoral dissertation: graduate work which involves research on human subjects or a clinical investigation and results in a thesis or dissertation.

Pilot studies: pilot studies involving human subjects are considered human subject research and require IRB review.

Clinical research: involves research to increase scientific understanding about normal or abnormal physiology, disease states or development and research to evaluate the safety, effectiveness or usefulness of a medical product, procedure, or intervention. Vaccine trials, medical device or drug studies and cancer research are all types of clinical research.

Behavioral and Social Sciences Research: focuses on individual and group behavior, mental processes, or social constructs and usually generates data by means of surveys, interviews, observations, studies of existing records, and experimental designs involving exposure to some type of stimulus or environmental intervention.

Epidemiological Research: focuses on health outcomes, interventions, disease states and conclusions about cost-effectiveness, efficacy, efficiency, interventions, or delivery of services to affected populations. This research may be conducted through surveillance, observation monitoring, and reporting programs. Other methods are retrospective review of medical, public health and/or other records.

Human Genetic Research: includes studies such as pedigree studies, positional cloning studies, gene transfer research, longitudinal studies to associate genetic conditions with health, health care or social outcomes and gene frequency studies.

Repository or Bank: includes collecting or storing human specimens or data for future use in research.

5. The following activities are generally not considered “research” and do not need IRB approval:

Health surveillance. Health surveillance is an ongoing part of the medical care and public health care functions closely integrated with timely dissemination of these data to those responsible for preventing and controlling disease or injury (may include emergent or urgently identified or suspected imminent health threats to the population to document the existence and magnitude).

Routine Quality Improvement (QI) means systematic, data-guided activities designed to bring about immediate, positive changes in the delivery of health care in particular settings. QI involves deliberate actions to improve care, guided by data reflecting the effects of local care (e.g., types of practical problem solving; an evidence-based management style; the application of science of how to bring about system change; review of aggregate data at the patient/provider/unit/ organizational level to identify a clinical or management change that can be expected to improve care).

Medical quality assurance. This refers to activities particular to an institution’s Quality Assurance (QA) program, such as those activities protected from disclosure by the Department of Veterans Affairs as part of its confidential medical quality-assurance program or other equivalent programs. (e.g., see VHA Directives or equivalent university or institutional policy)

Program evaluation. This refers to assessments of the success of established programs in achieving objectives when the assessments are for the use of program managers, for example, a survey to determine if program beneficiaries are aware of the availability of program services or benefits. [Note: Non-research evaluation is generally designed to assess or improve the program or service rather than to generate knowledge about a disease or condition.]

Customer satisfaction surveys or interviews. This refers to surveys of program users to obtain feedback for use by program managers, and is similar to program evaluation. The purpose of these surveys is to improve a specific service or program or develop new services or programs under the control of the individual/organization obtaining the information and not to conduct research.

Class Projects: academic projects or student assignments involving collection of data from human subjects when the data is used solely for the purpose of teaching course content (e.g., to teach proficiency in performing certain tasks or using specific tools or methods) and not intended to be used to develop or contribute to generalizable knowledge.

Case Reports: use of medical information collected from a clinical activity rather than a research activity and presented on no more than three (3) patients. Case reports are generally done by retrospective review of the medical record and highlights a unique treatment, case or outcome. The examination of the case is usually not systematic and there is usually no data analysis or testing of a hypothesis. Investigators must ensure that the HIPAA privacy rules are followed with respect to using or accessing PHI (a HIPAA authorization or waiver may be required).

Biography or oral history of a single individual: research involving a single individual is not generalizable knowledge. (see precautions in case reports)

Publicly Available Data: research involving publicly available information (e.g., census data, labor statistics) does not constitute human research.

6. The following research is generally not considered “human research” and do not need approval:

Repository Research, Tissue Banking, and Databases: research limited to obtaining stored data or specimens from a repository only if the investigator cannot readily ascertain the identity of the subject from whom the data or materials originated.

Anonymous Pre-existing Data Sets or Specimens: anonymous pre-existing data or specimens (anonymous materials are those with no personally identifiable information contained in either the original data or attached to the original specimen).

Coded pre-existing or coded prospective data or specimens: if 1) the private information/specimens were not/will not be collected specifically for the currently proposed research through an interaction or intervention with living individuals, or 2) the investigator(s) never obtains identifiable data/specimens because: a) the holder of the key to decipher the code, destroys the key before the data is provided to the investigator, or b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, or until the individuals are deceased; or c) there are laws or IRB-approved written policies for a repository/data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased.